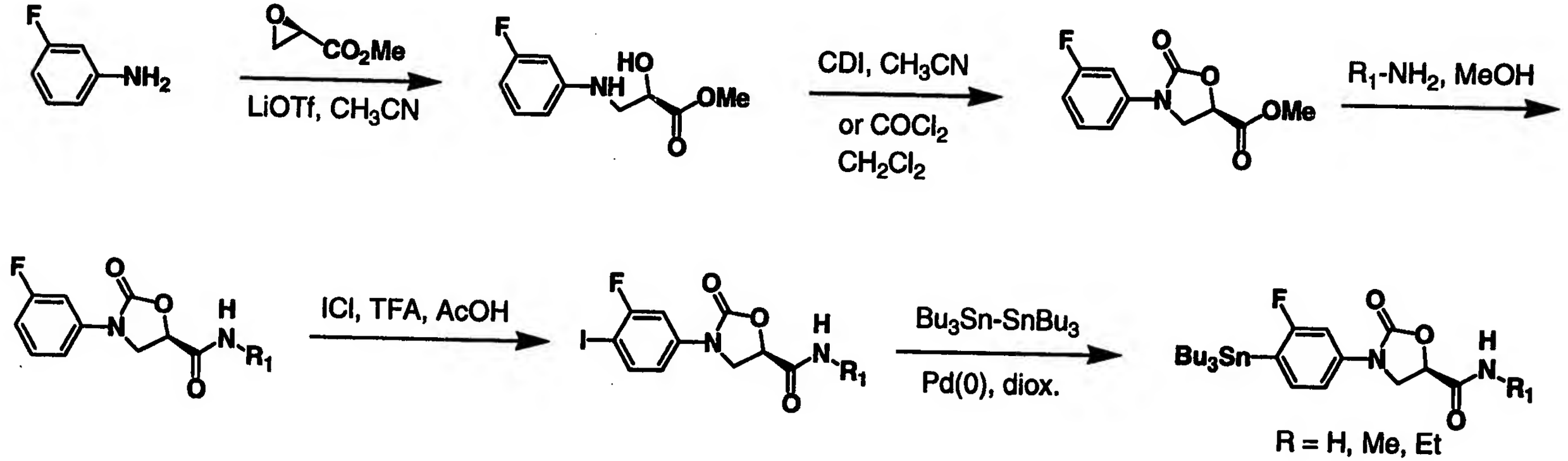
FIGURE I

C-5 Carboxamides



C-5 Ester

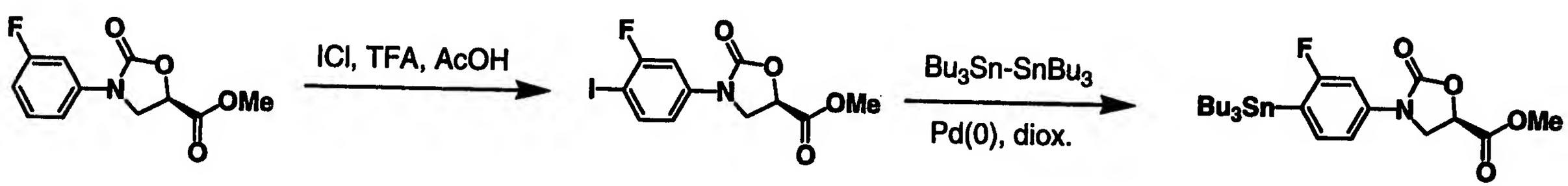


FIGURE II

Synthetic Routes to Key Heterocyclic Pyridines/Pyrimidines

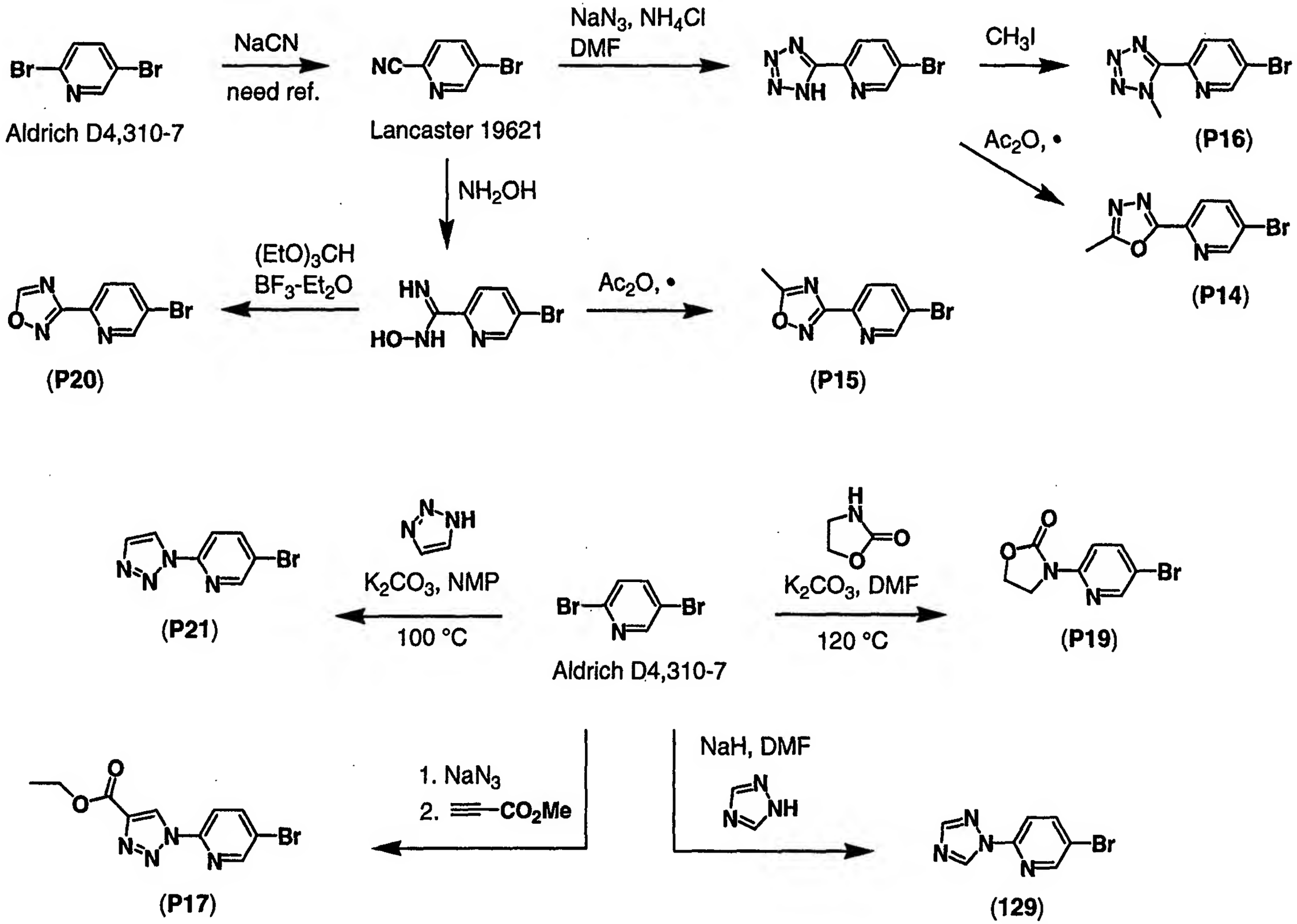
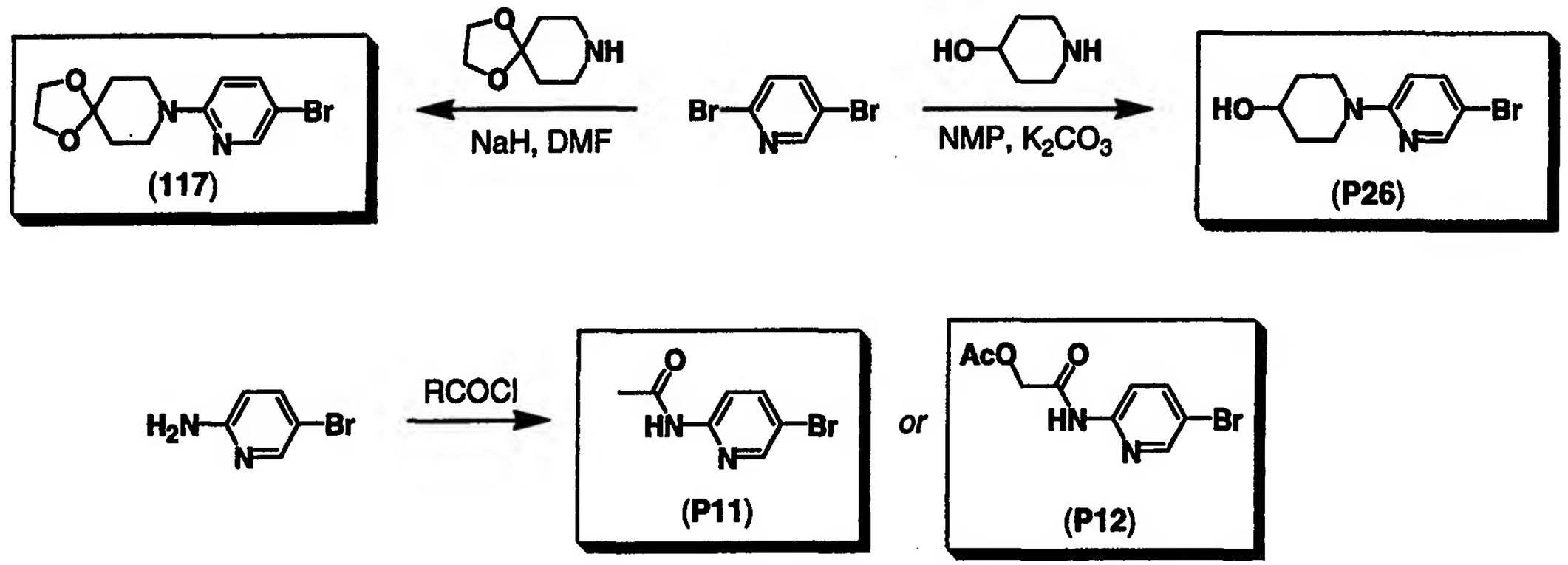
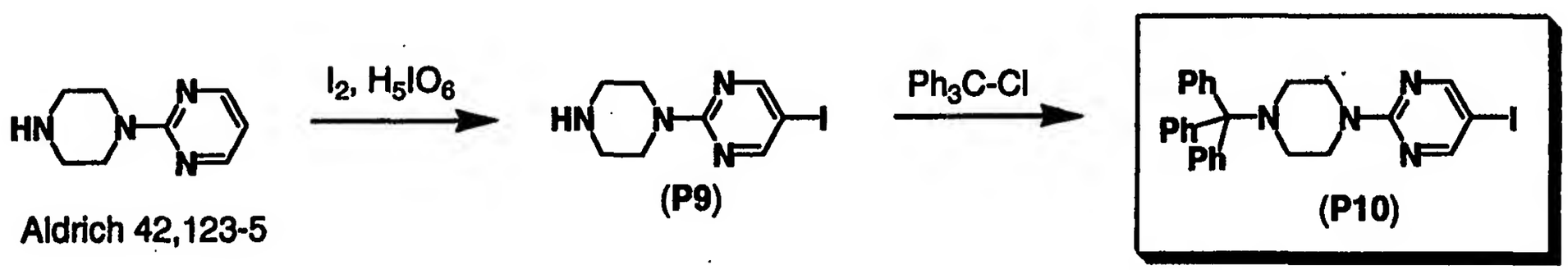


FIGURE III

Synthetic Routes to Key Heterocyclic Pyridines/Pyrimidines





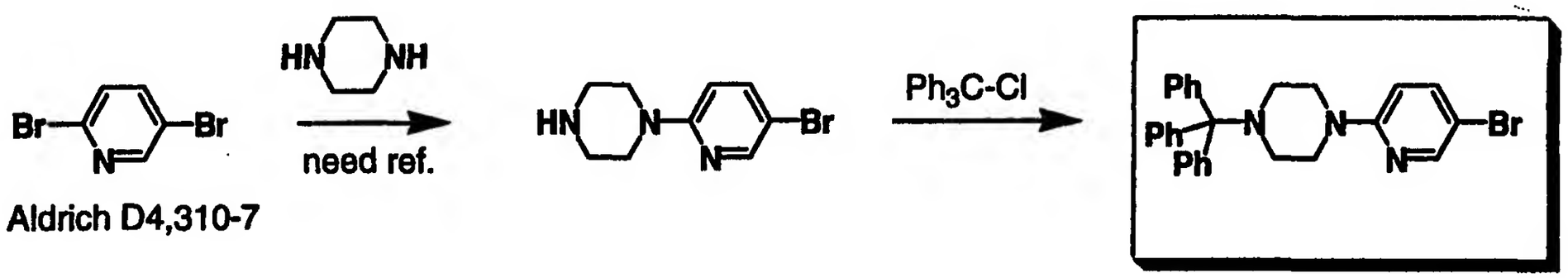


FIGURE IV

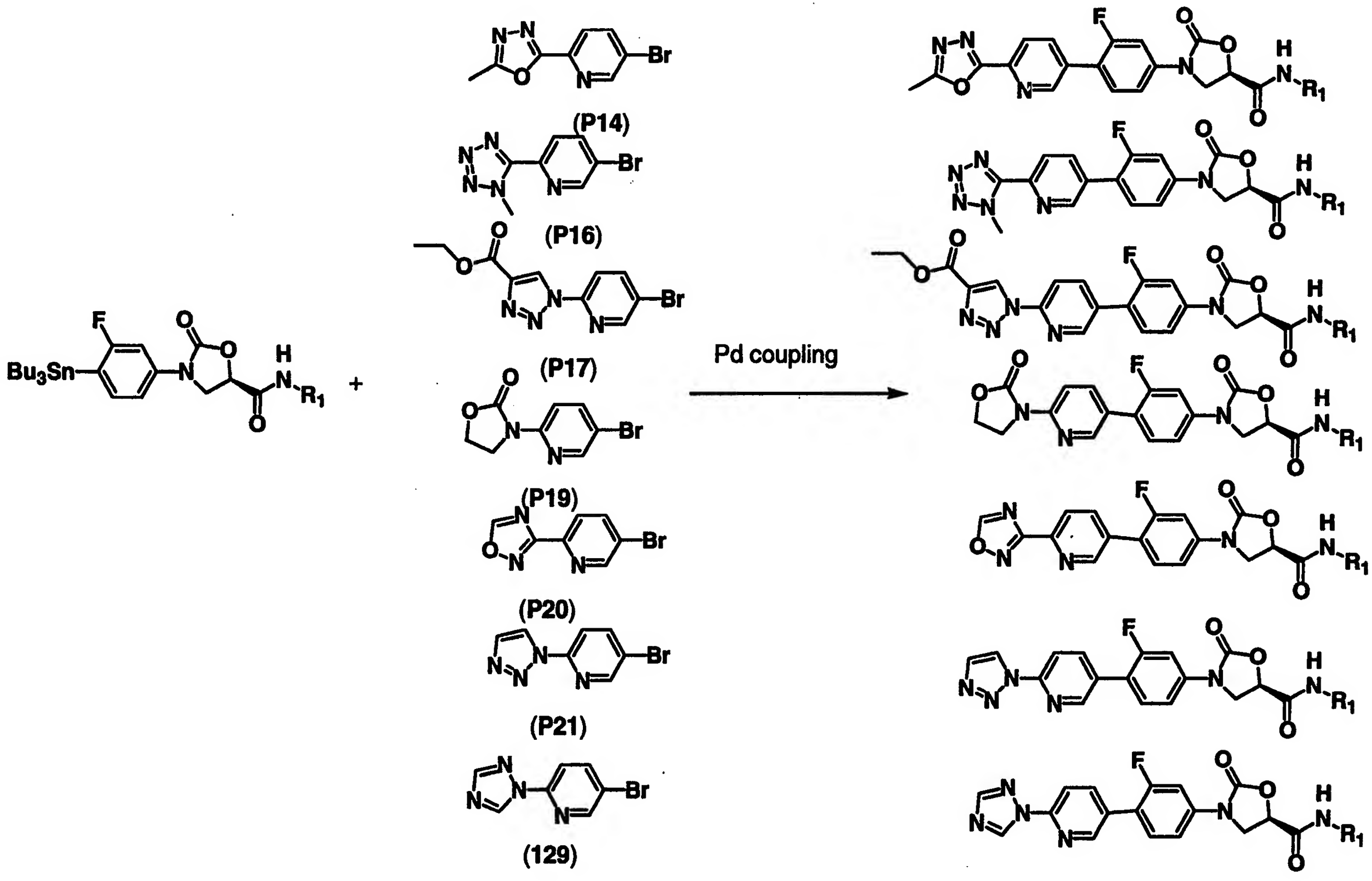


FIGURE V

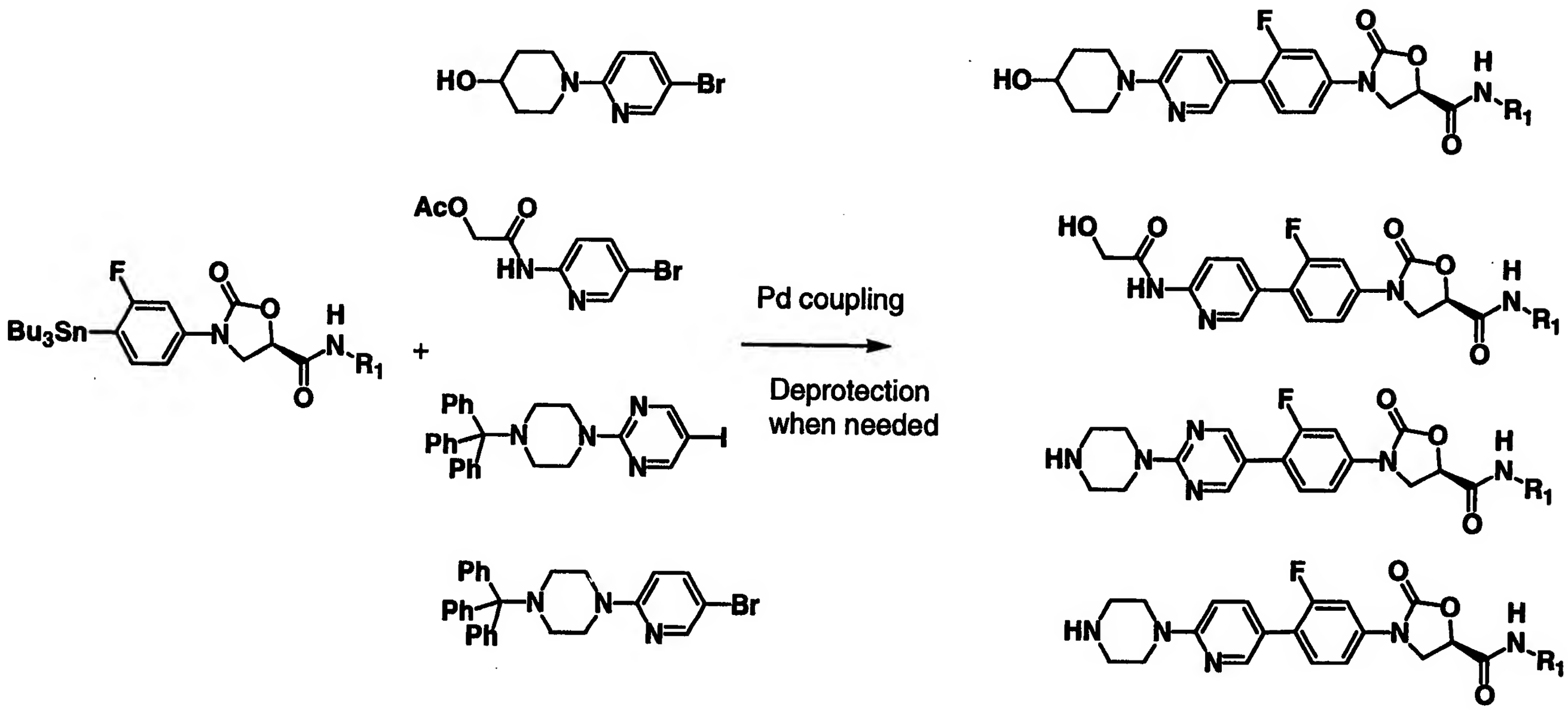


FIGURE VI

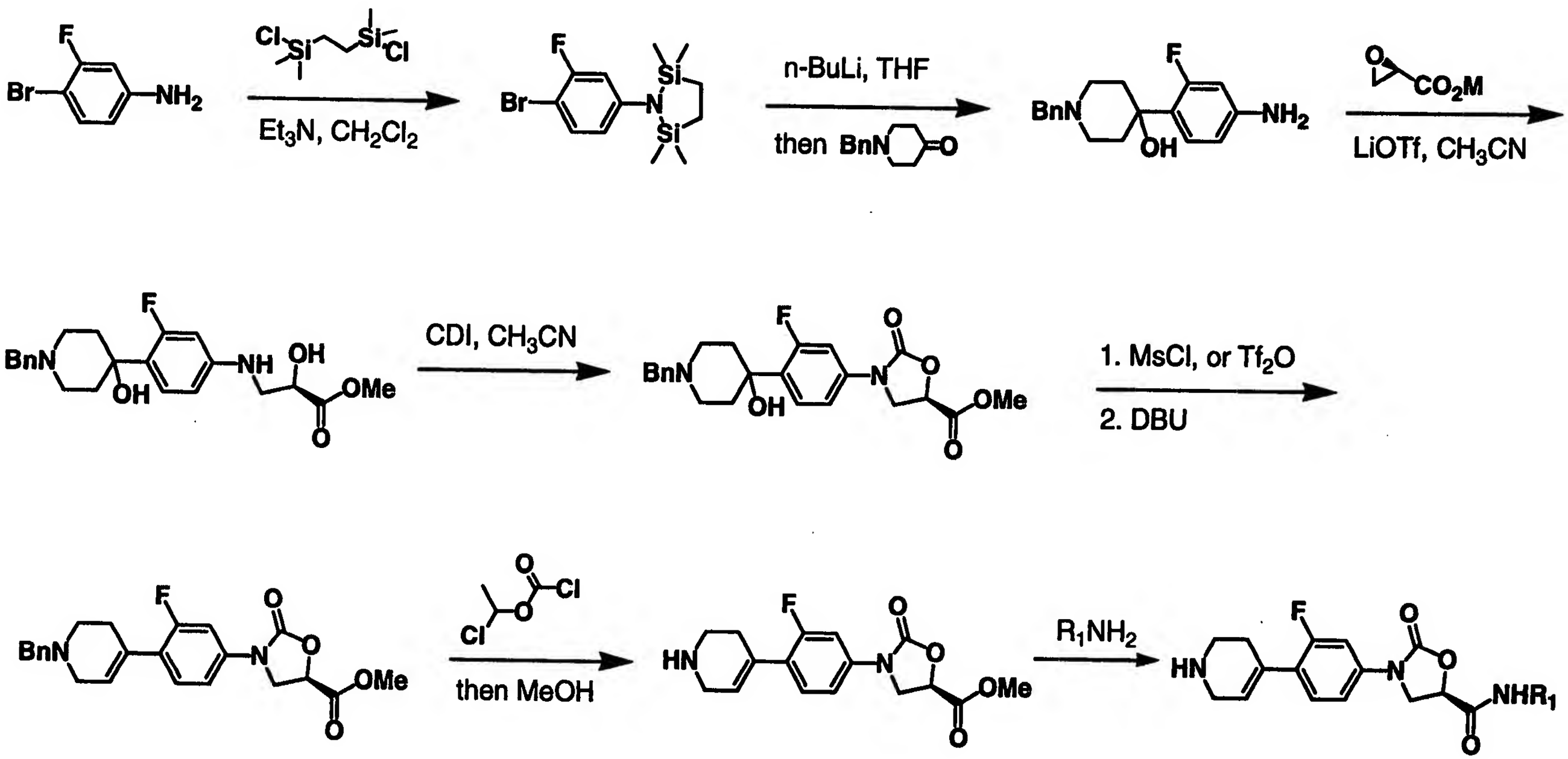
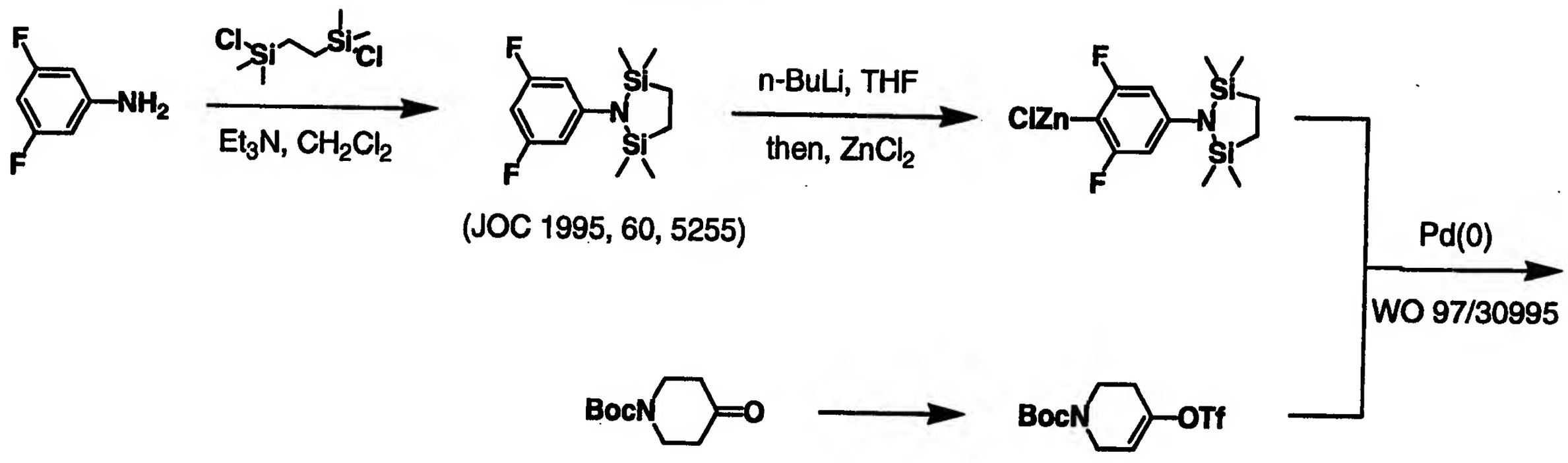

F
Br
NH2
Cl
Si
Si
Cl
Et3N, CH2Cl2
n-BuLi, THF
then BnN=O
BnN
OH
CO2M
LiOTf, CH3CN
NH
OMe
CDI, CH3CN
1. MsCl, or Tf2O
2. DBU
Cl
then MeOH
HN
R1NH2
NHR1

FIGURE VII


F
NH2
F
Cl
Si
Si
Cl
Et3N, CH2Cl2
F
Si
N
Si
F
n-BuLi, THF
then, ZnCl2
ClZn
F
Si
N
Si
F
(JOC 1995, 60, 5255)
Pd(0)
WO 97/30995
BocN
O
BocN
OTf
(Synthesis 1991, 993)

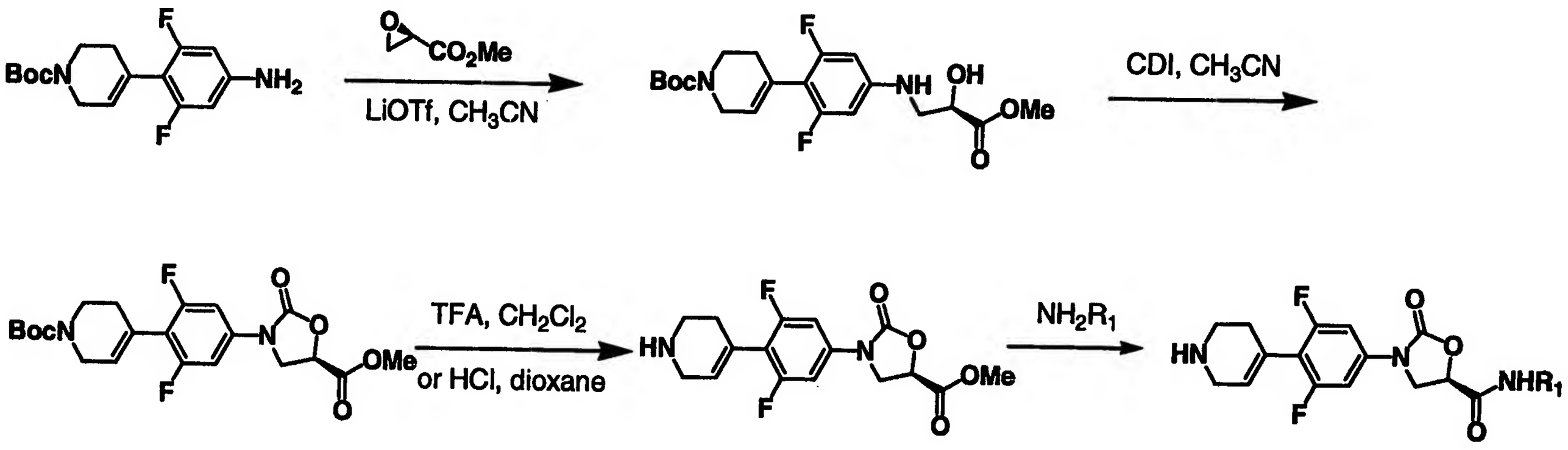
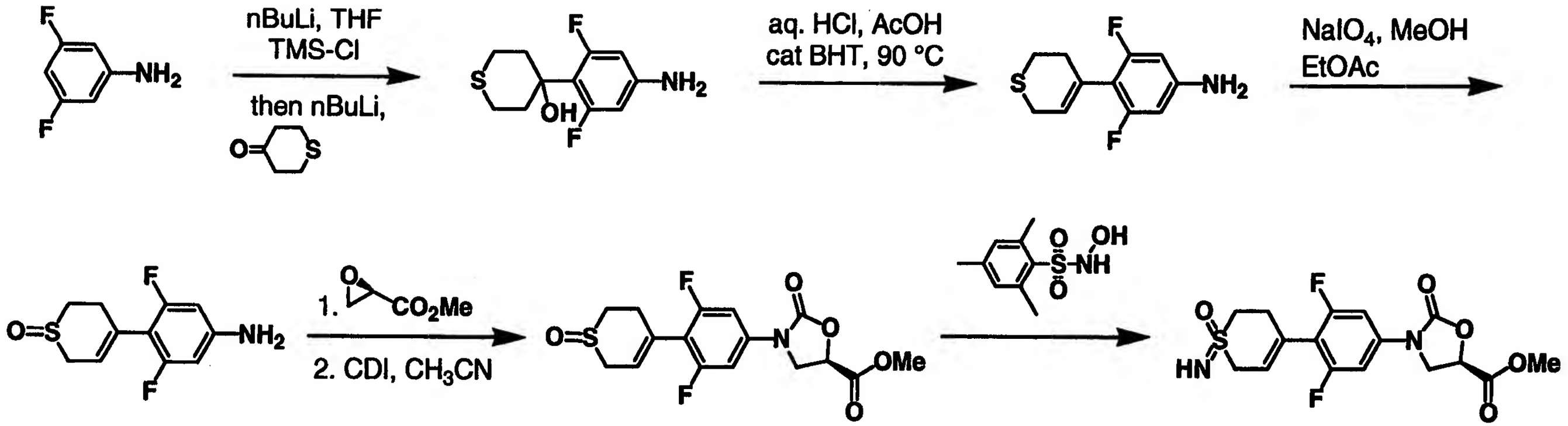

F
BocN
NH2
F
O
CO2Me
LiOTf, CH3CN
F
BocN
NH
OH
OMe
O
F
CDI, CH3CN
F
BocN
O
N
O
OMe
F
O
TFA, CH2Cl2
or HCl, dioxane
F
HN
O
N
O
OMe
F
O
NH2R1
F
HN
O
N
O
NHR1
F
O

FIGURE VIII



Alternate route:

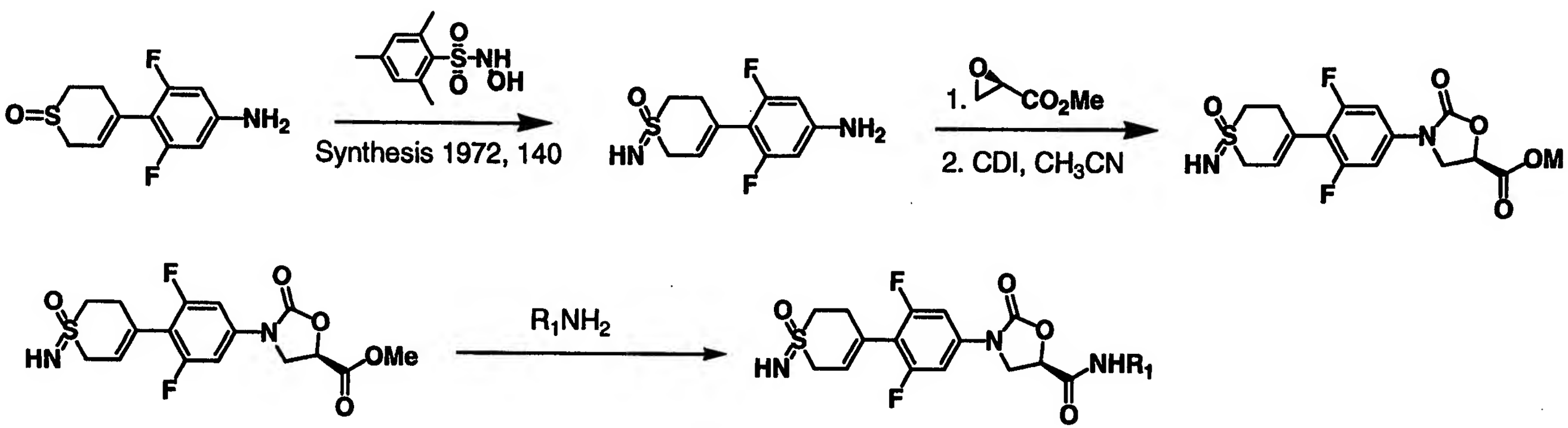


FIGURE IX

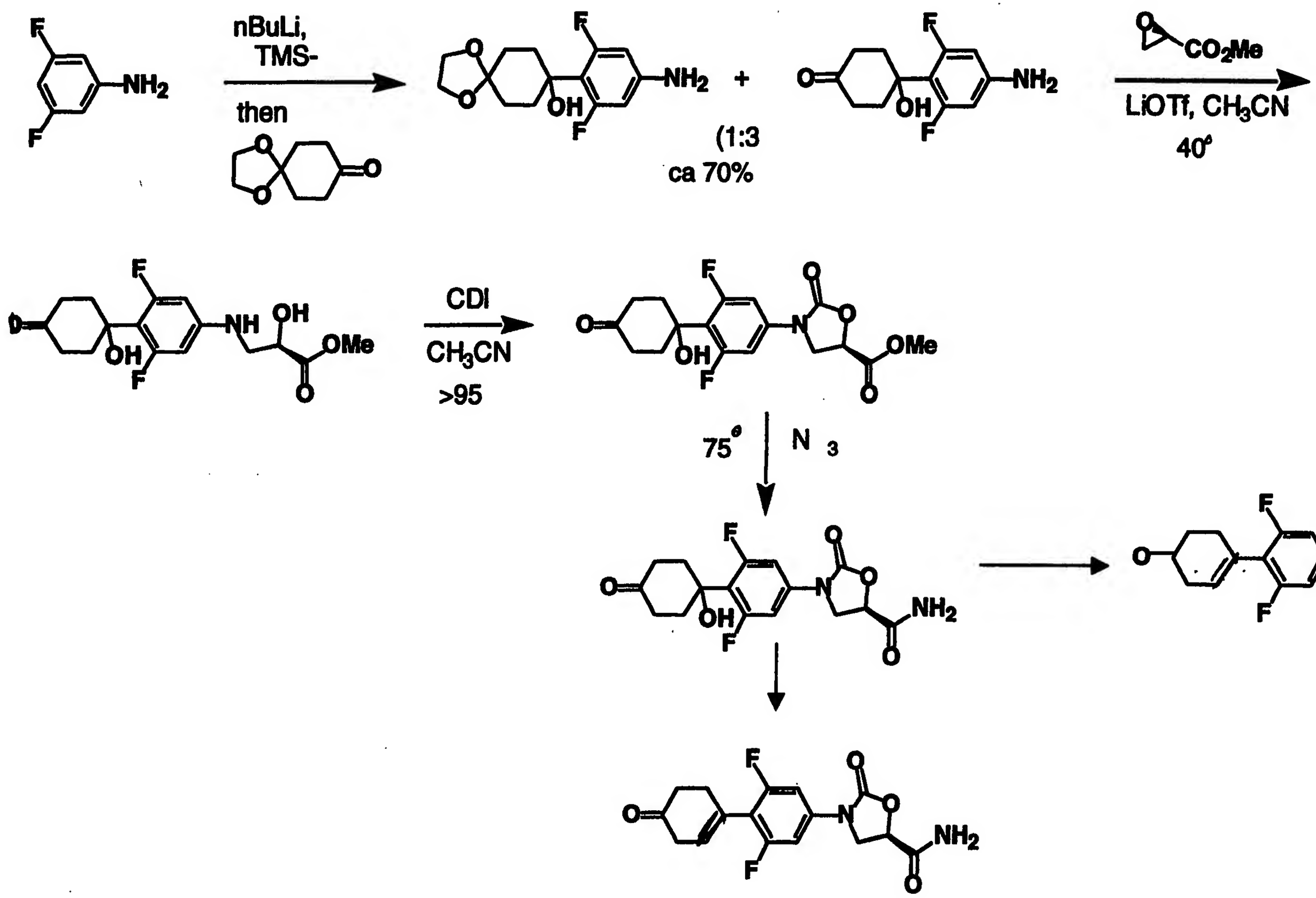


FIGURE X

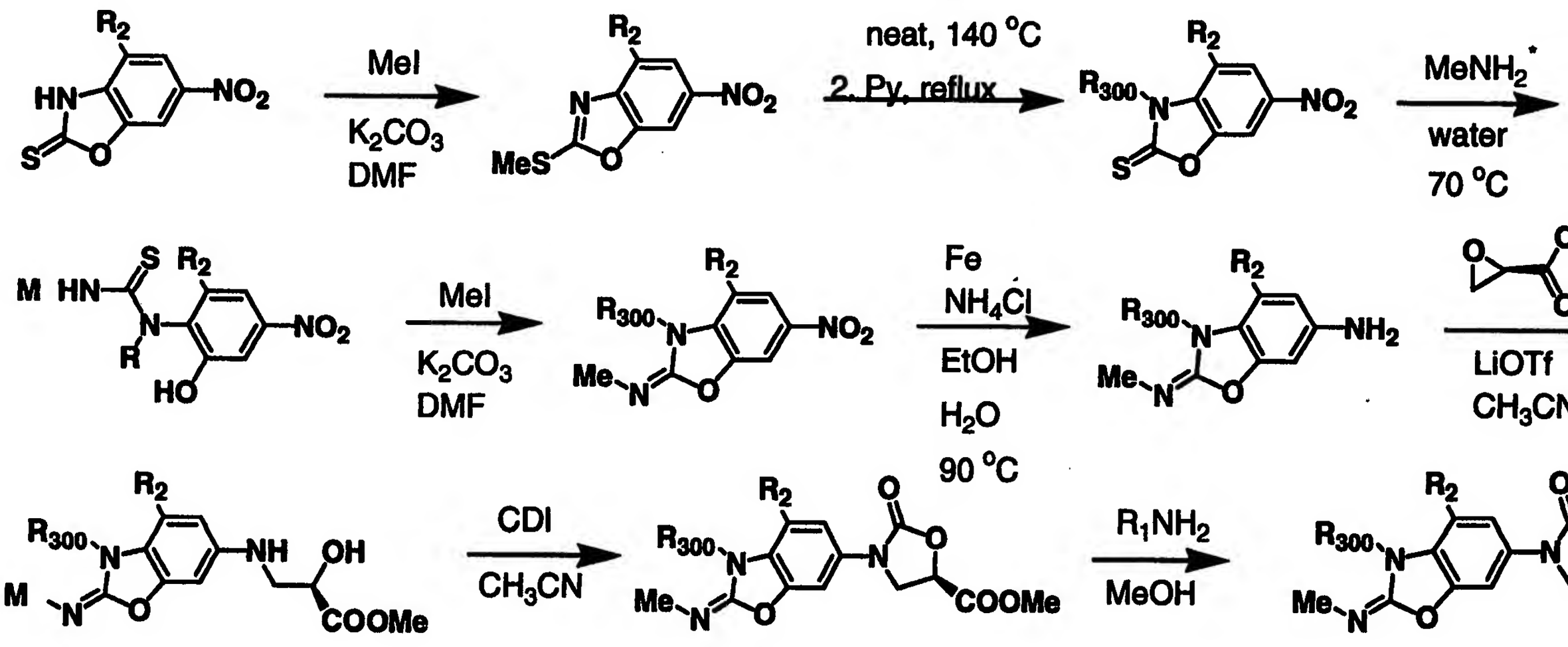

R2
HN
NO2
S
O
MeI
K2CO3
DMF
MeS
N
1.TolSO2R
neat, 140 °C
2. Py, reflux
R300
MeNH2*
water
70 °C
M
HN
S
R2
N
R
HO
NO2
Fe
NH4Cl
EtOH
H2O
90 °C
Me
NH2
OM
LiOTf
CH3CN
NH
OH
COOMe
CDI
R1NH2
MeOH
H
R1

FIGURE XI

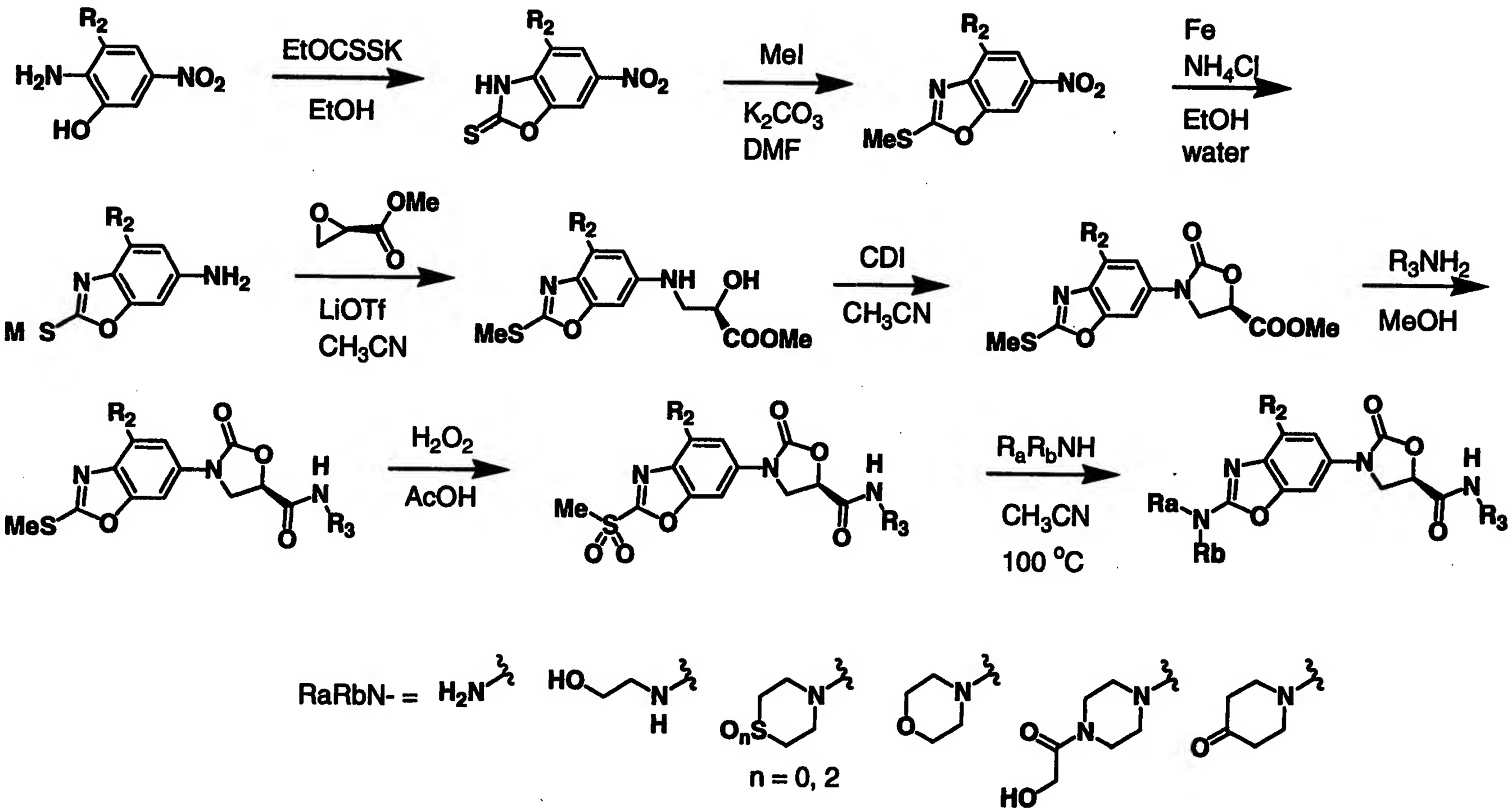

EtOCSSK
EtOH
MeI
K_2CO_3
DMF
Fe
NH_4Cl
EtOH
water
LiOTf
CH_3CN
CDI
CH_3CN
R_3NH_2
MeOH
H_2O_2
AcOH
R_aR_bNH
CH_3CN
100 °C
RaRbN- =
n = 0, 2

FIGURE XII

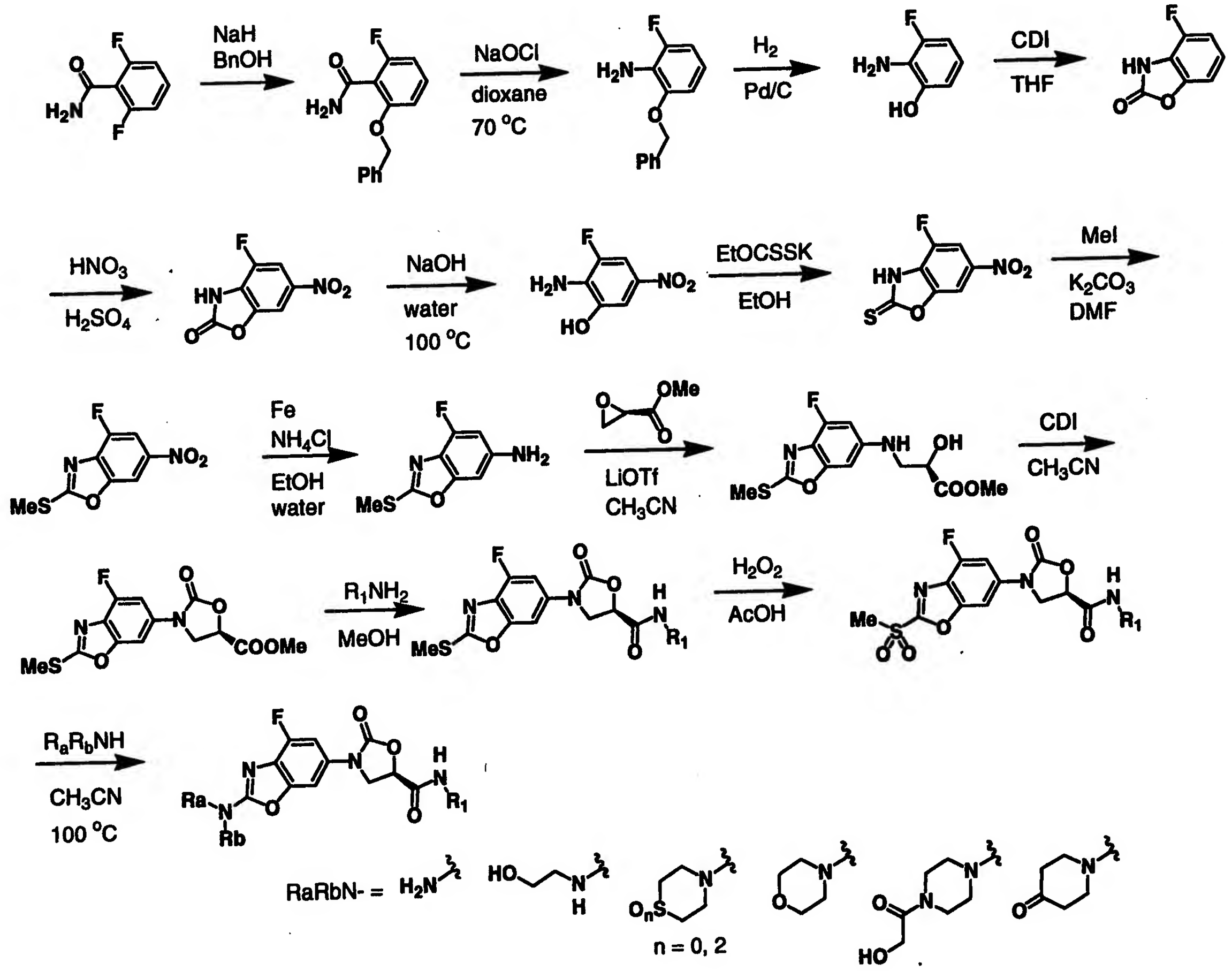

NaH
BnOH
NaOCl
dioxane
70 °C
H2
Pd/C
CDI
THF
HNO3
H2SO4
NaOH
water
100 °C
EtOCSSK
EtOH
MeI
K2CO3
DMF
Fe
NH4Cl
EtOH
water
LiOTf
CH3CN
CDI
CH3CN
R1NH2
MeOH
H2O2
AcOH
RaRbNH
CH3CN
100 °C
RaRbN- =
n = 0, 2

FIGURE XIII

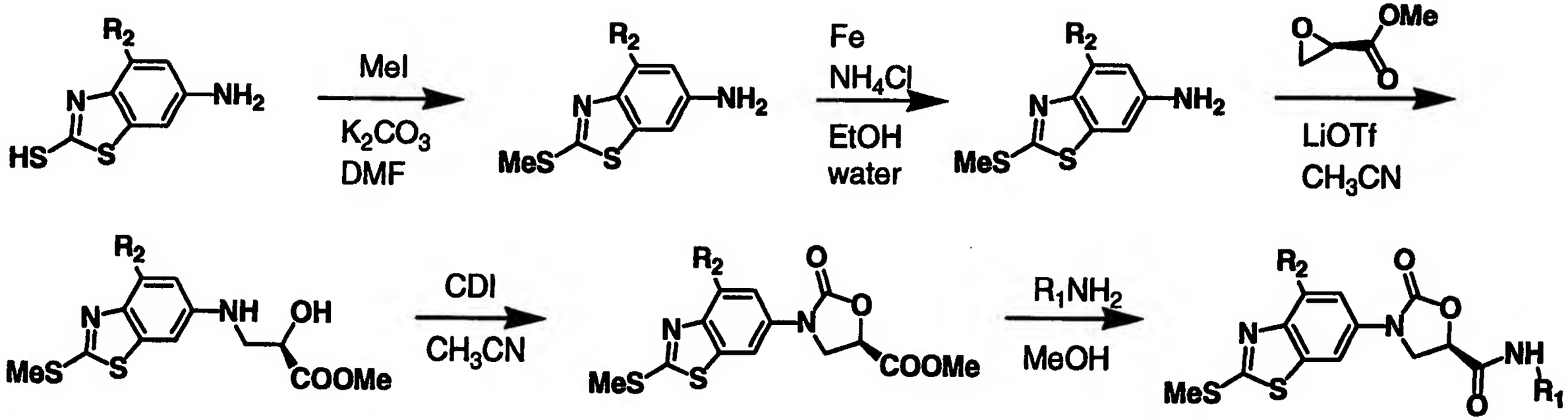

MeI
K2CO3
DMF
Fe
NH4Cl
EtOH
water
LiOTf
CH3CN
CDI
CH3CN
R1NH2
MeOH
H2O2
AcOH
RaRbNH
CH3CN
100 °C
RaRbN- =
n = 0, 2

FIGURE X I V

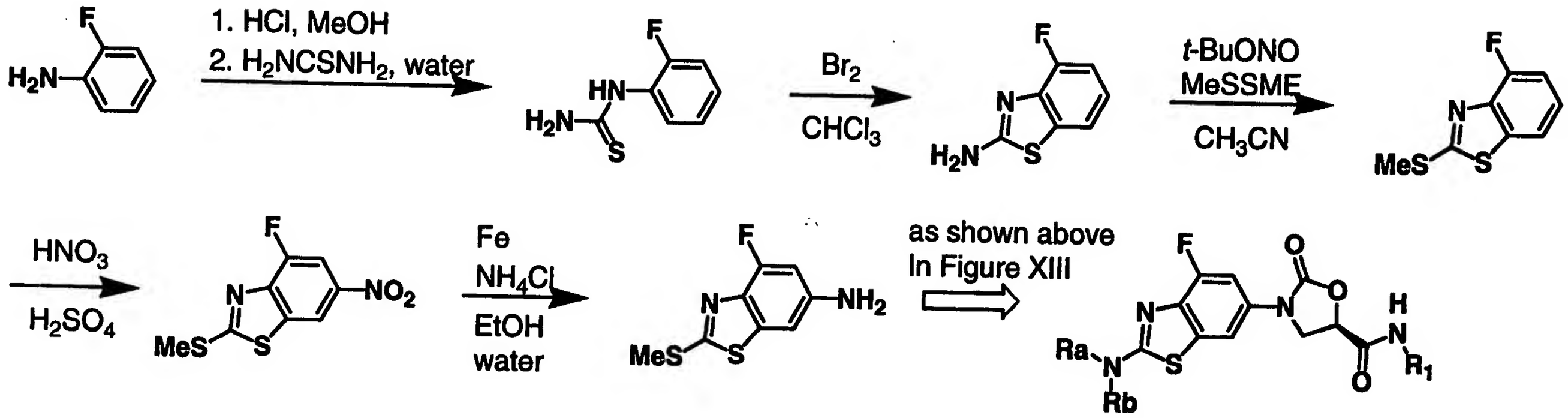
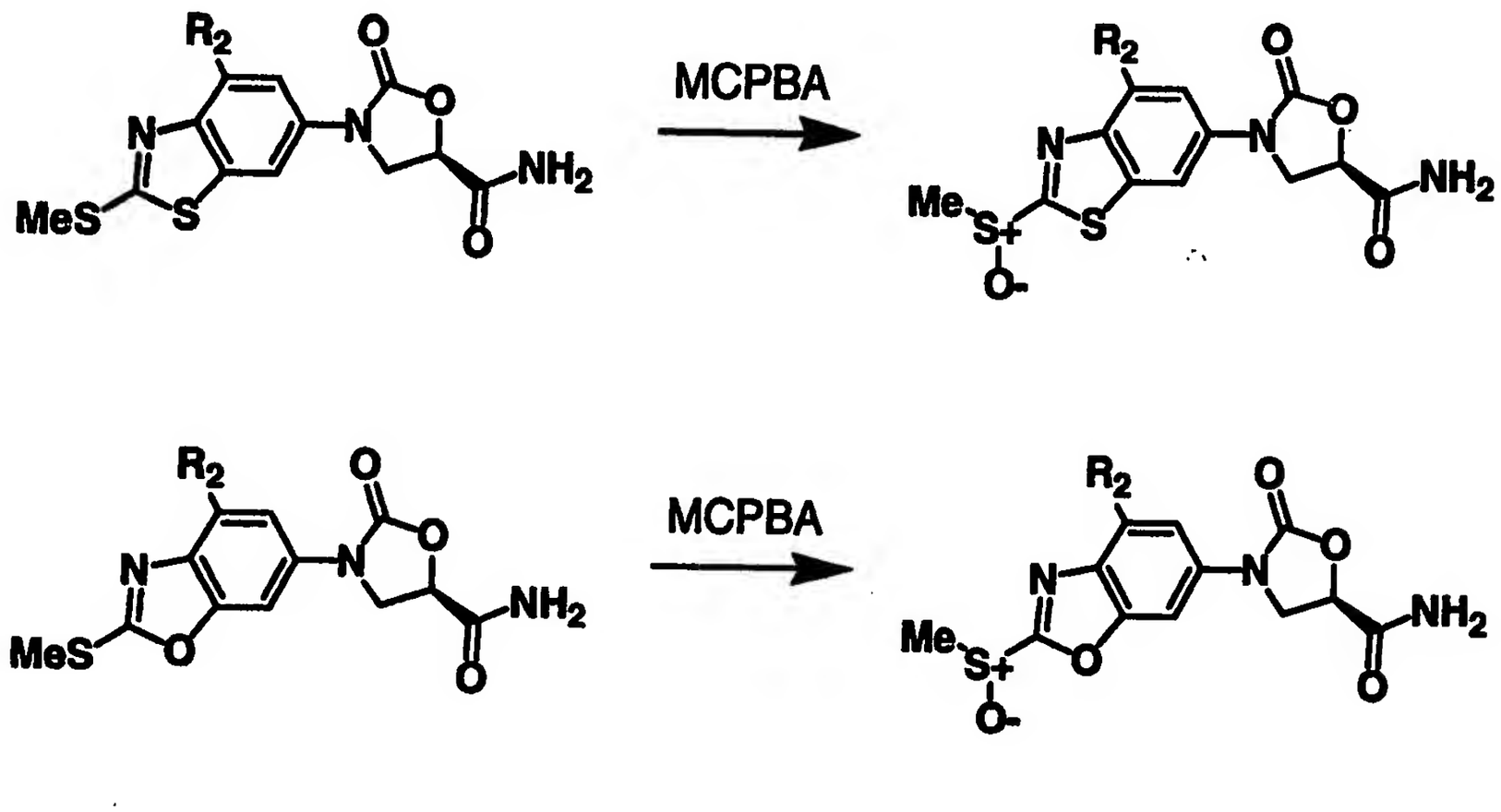

F
H2N
1. HCl, MeOH
2. H2NCSNH2, water
HN
H2N
S
Br2
CHCl3
N
H2N
S
t-BuONO
MeSSME
CH3CN
MeS
HNO3
H2SO4
NO2
Fe
NH4Cl
EtOH
water
NH2
as shown above
In Figure XIII
O
O
H
N
R1
Ra
N
Rb

FIGURE XV


R2
O
N
O
NH2
MeS
S
O
MCPBA
Me
S+
O-

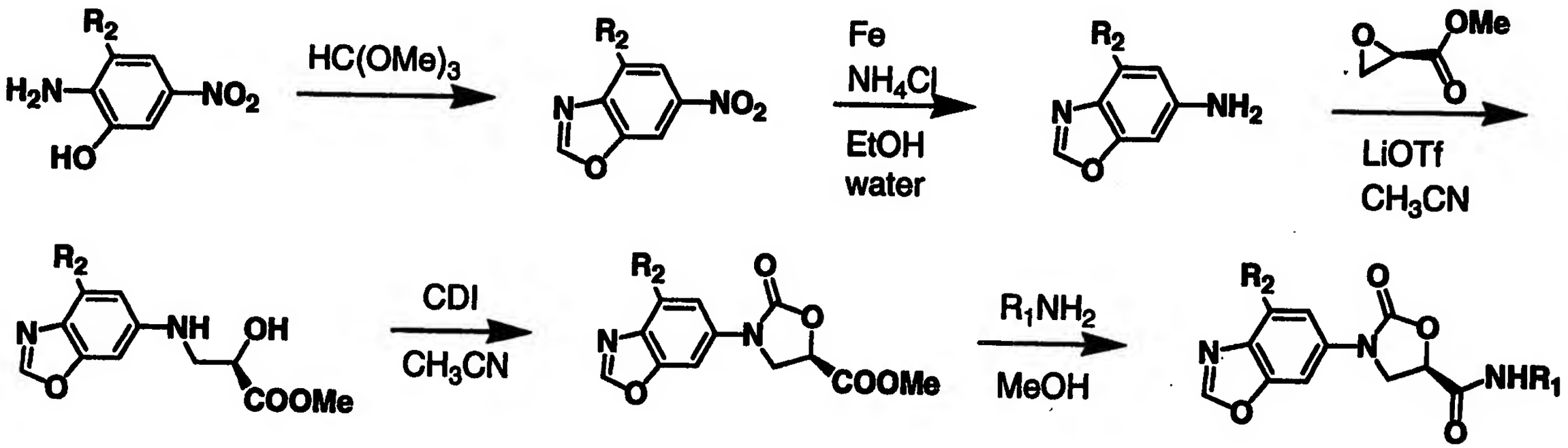

R2
H2N
NO2
HO
HC(OMe)3
Fe
NH4Cl
EtOH
water
NH2
OMe
LiOTf
CH3CN
NH
OH
COOMe
CDI
CH3CN
R1NH2
MeOH
NHR1

FIGURE XVI

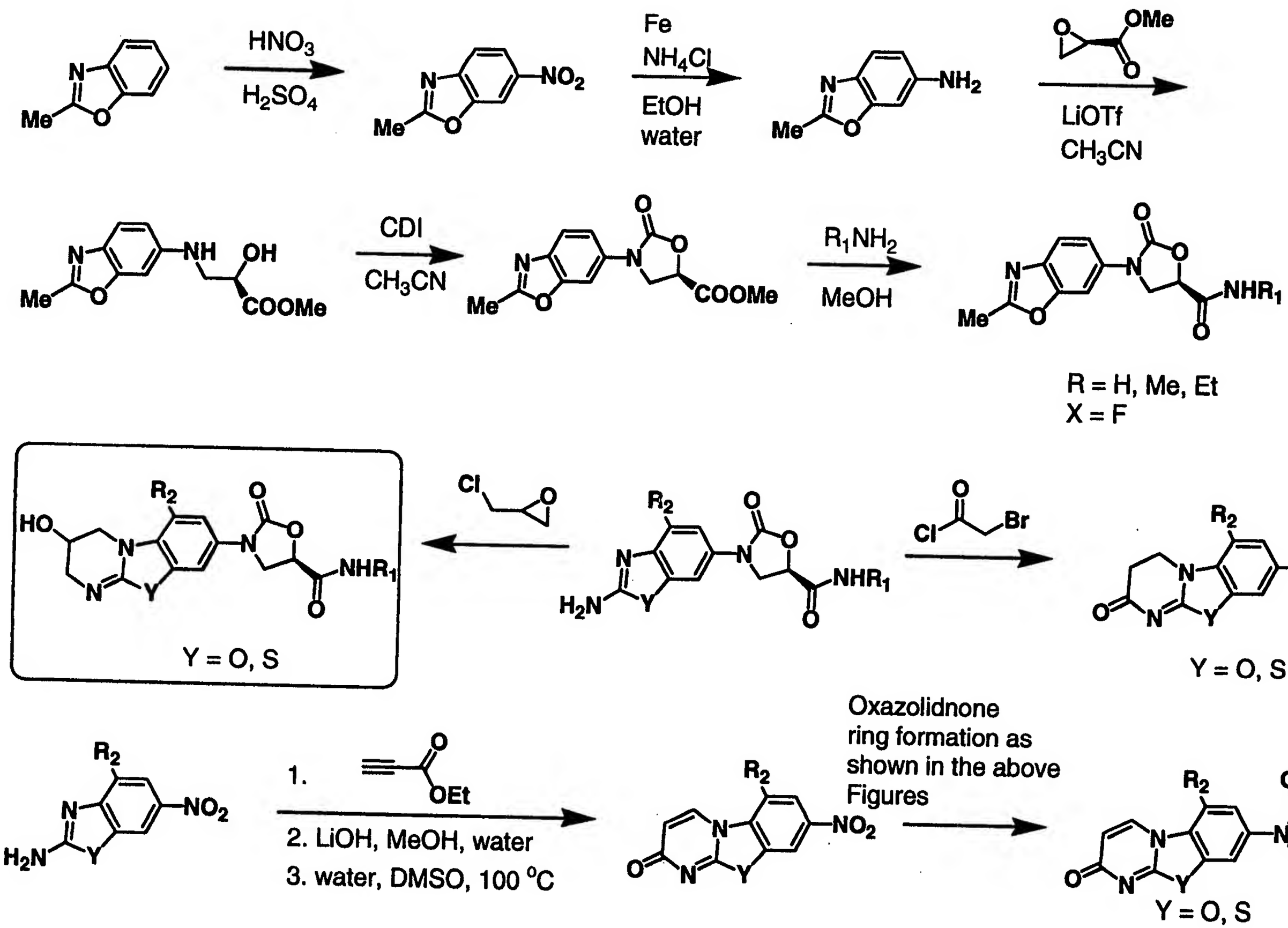

HNO3
H2SO4
Fe
NH4Cl
EtOH
water
LiOTf
CH3CN
CDI
CH3CN
R1NH2
MeOH
R = H, Me, Et
X = F
Y = O, S
1.
2. LiOH, MeOH, water
3. water, DMSO, 100 °C
Oxazolidnone ring formation as shown in the above Figures
Y = O, S

FIGURE XVII

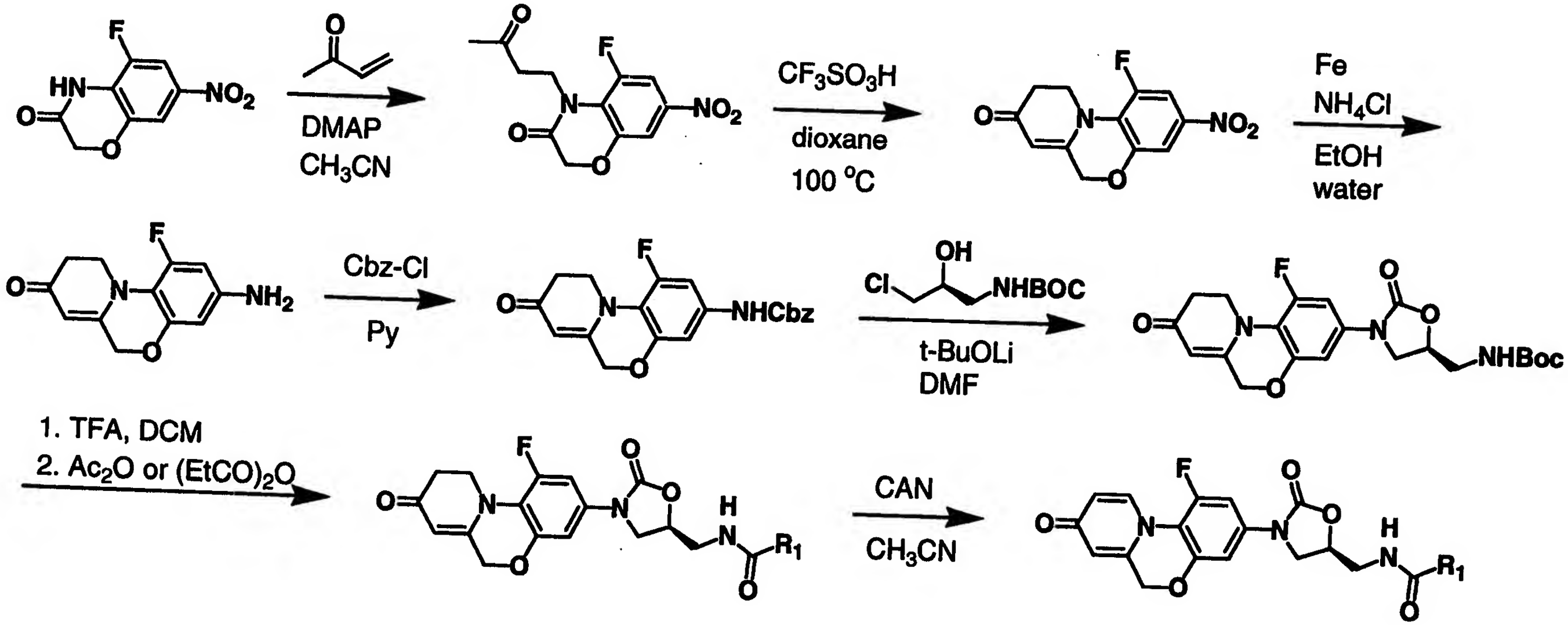

DMAP
CH3CN
CF3SO3H
dioxane
100 °C
Fe
NH4Cl
EtOH
water
Cbz-Cl
Py
t-BuOLi
DMF
1. TFA, DCM
2. Ac2O or (EtCO)2O
CAN
CH3CN

FIGURE XVIII

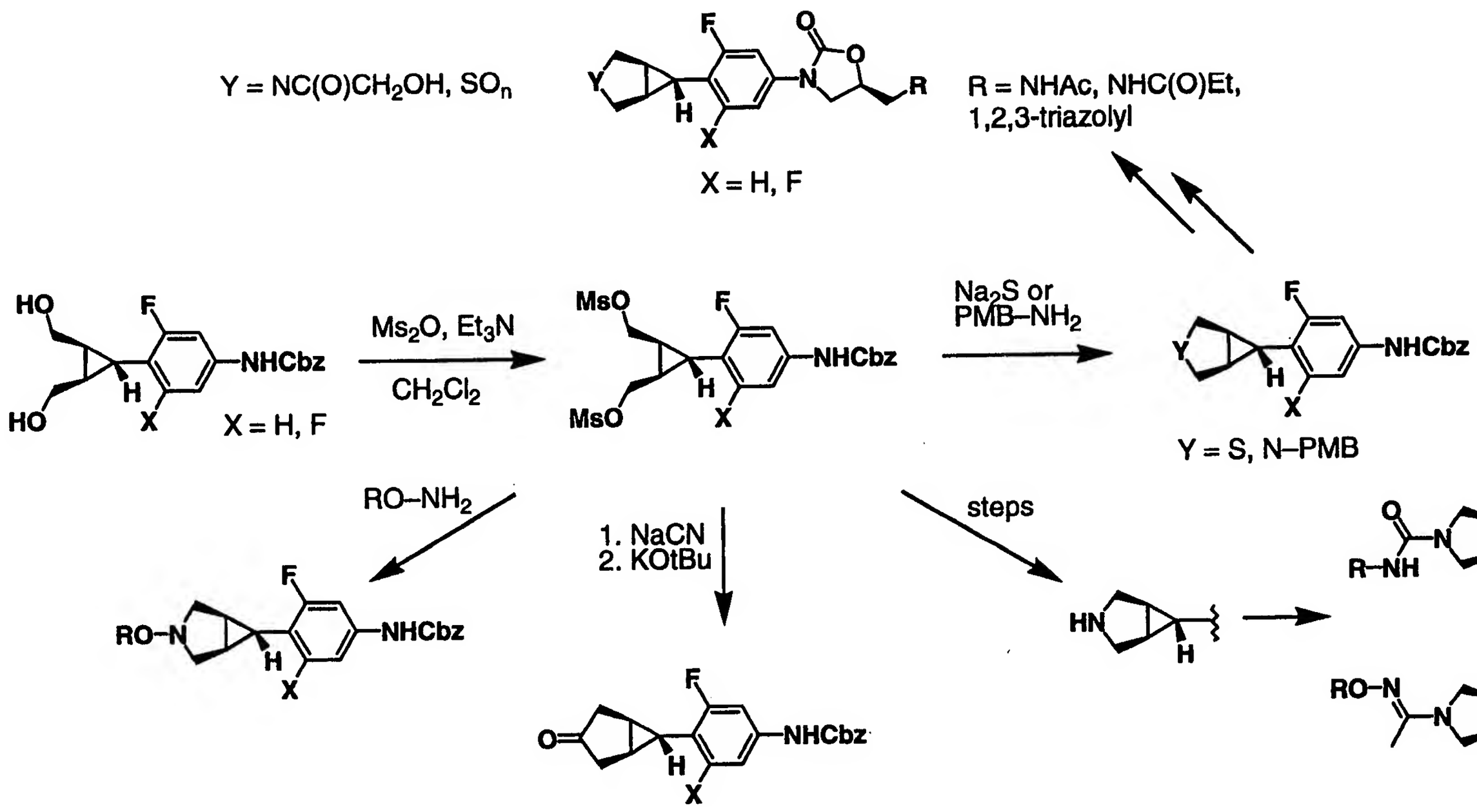


FIGURE XIX

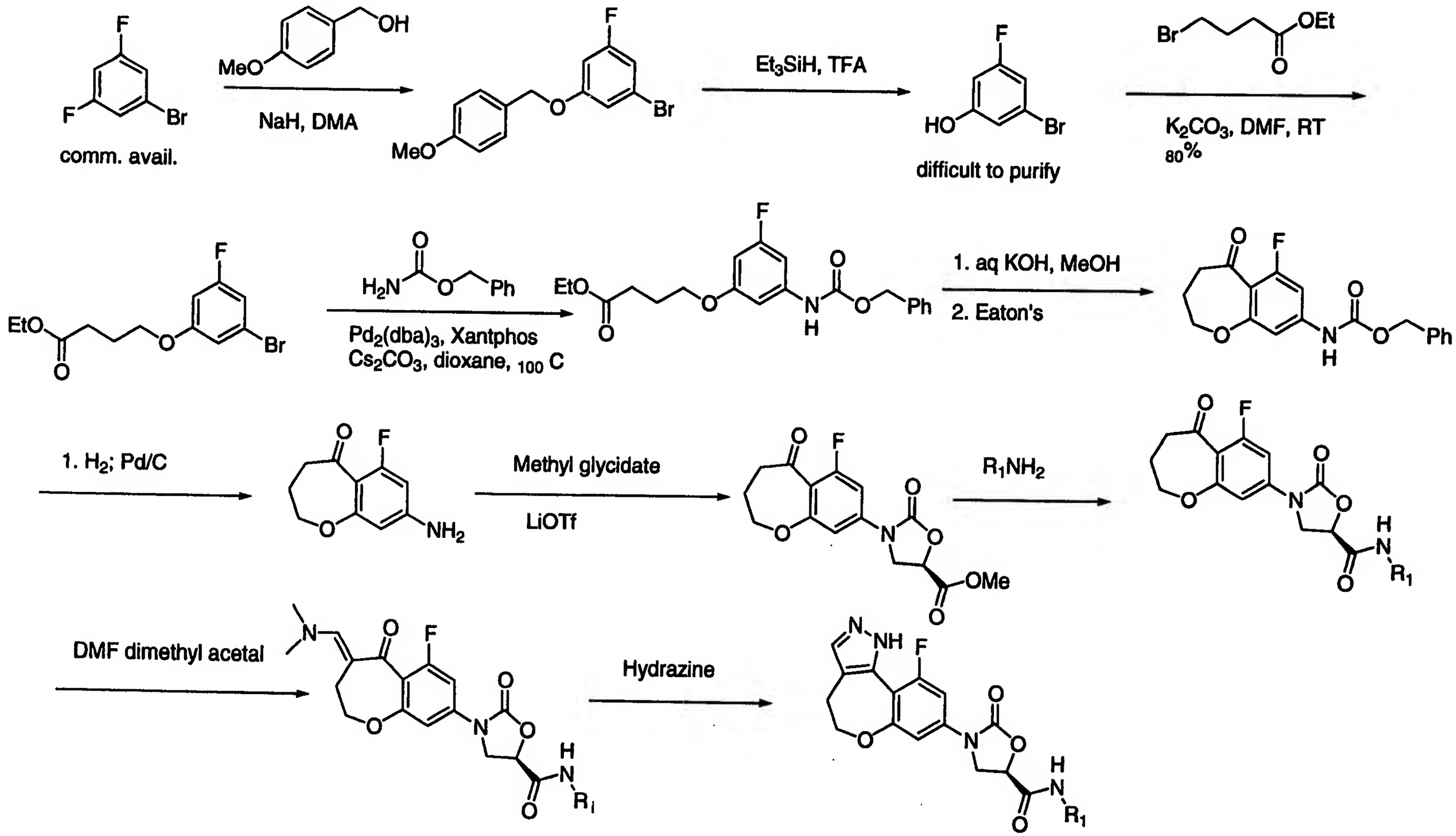

F
F
Br
comm. avail.
MeO
OH
NaH, DMA
MeO
F
Br
Et3SiH, TFA
HO
F
Br
difficult to purify
Br
OEt
O
K2CO3, DMF, RT
80%
EtO
O
F
Br
H2N
O
O
Ph
Pd2(dba)3, Xantphos
Cs2CO3, dioxane, 100 C
EtO
O
F
O
N
H
O
Ph
1. aq KOH, MeOH
2. Eaton's
O
F
O
N
H
O
Ph
1. H2; Pd/C
O
F
NH2
O
Methyl glycidate
LiOTf
O
F
O
N
O
O
OMe
R1NH2
O
F
O
N
O
H
N
R1
DMF dimethyl acetal
N
O
F
O
N
O
H
N
R1
Hydrazine
N
NH
F
O
N
O
H
N
R1

FIGURE XX

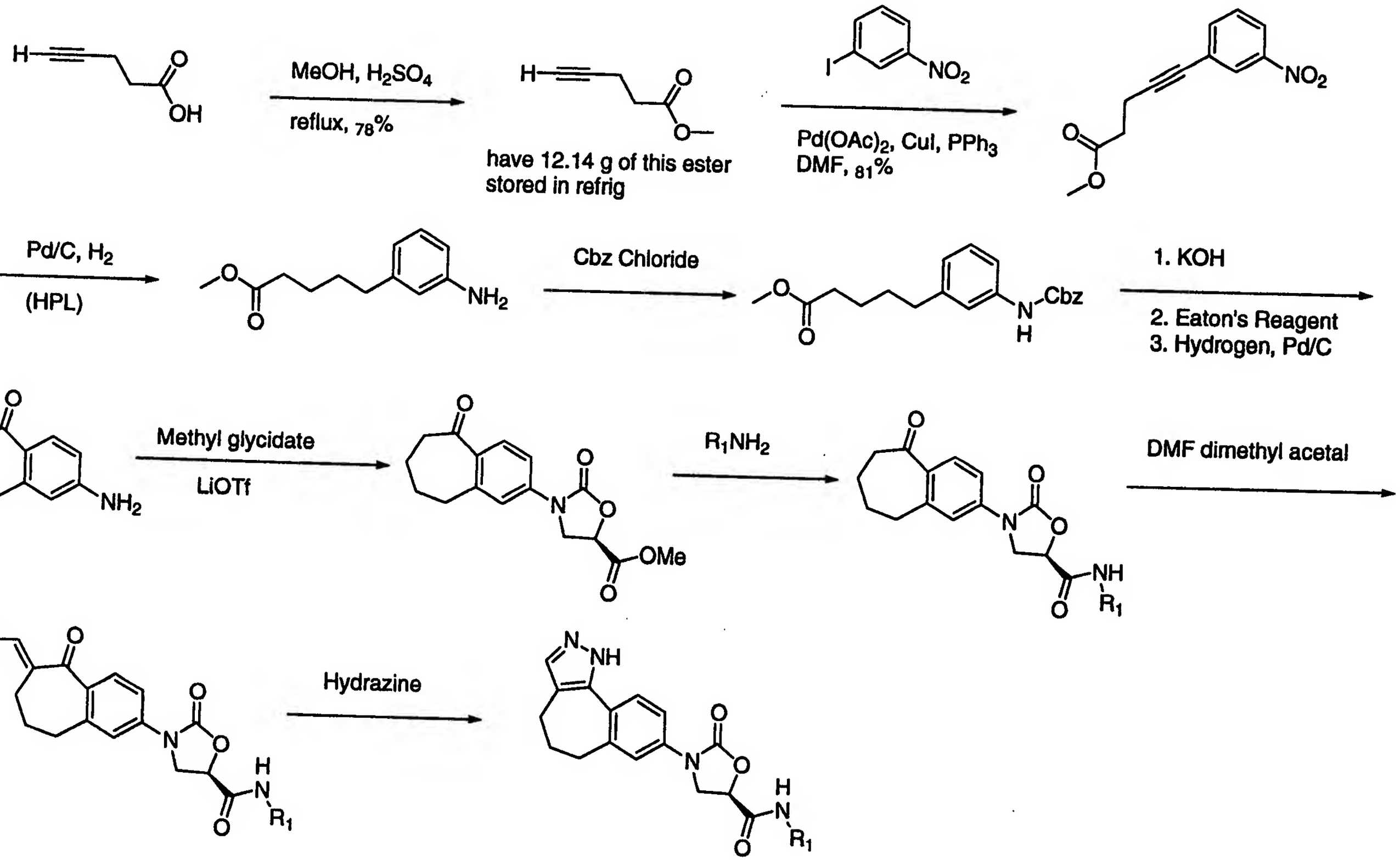

MeOH, H_2SO_4
reflux, 78%
have 12.14 g of this ester stored in refrig
$Pd(OAc)_2$, CuI, PPh_3
DMF, 81%
Pd/C, H_2
(HPL)
Cbz Chloride
1. KOH
2. Eaton's Reagent
3. Hydrogen, Pd/C
Methyl glycidate
LiOTf
R_1NH_2
DMF dimethyl acetal
Hydrazine

FIGURE XXI

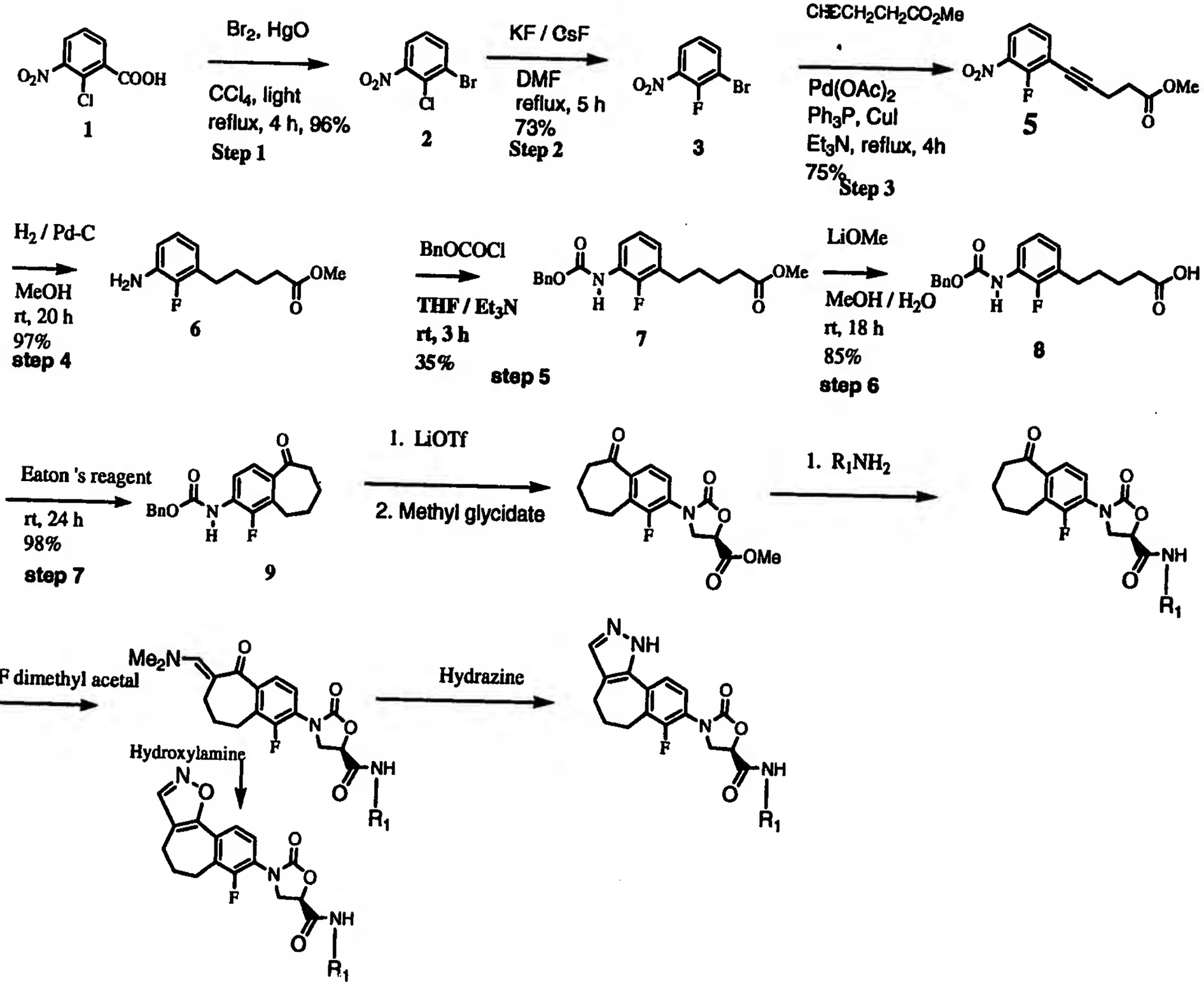

Br2, HgO
CCl4, light
reflux, 4 h, 96%
Step 1
KF / CsF
DMF
reflux, 5 h
73%
Step 2
CH≡CCH2CH2CO2Me
Pd(OAc)2
Ph3P, CuI
Et3N, reflux, 4h
75%
Step 3
H2 / Pd-C
MeOH
rt, 20 h
97%
step 4
BnOCOCl
THF / Et3N
rt, 3 h
35%
step 5
LiOMe
MeOH / H2O
rt, 18 h
85%
step 6
Eaton 's reagent
rt, 24 h
98%
step 7
1. LiOTf
2. Methyl glycidate
1. R1NH2
DMF dimethyl acetal
Hydroxylamine
Hydrazine
1
2
3
5
6
7
8
9

FIGURE XXII

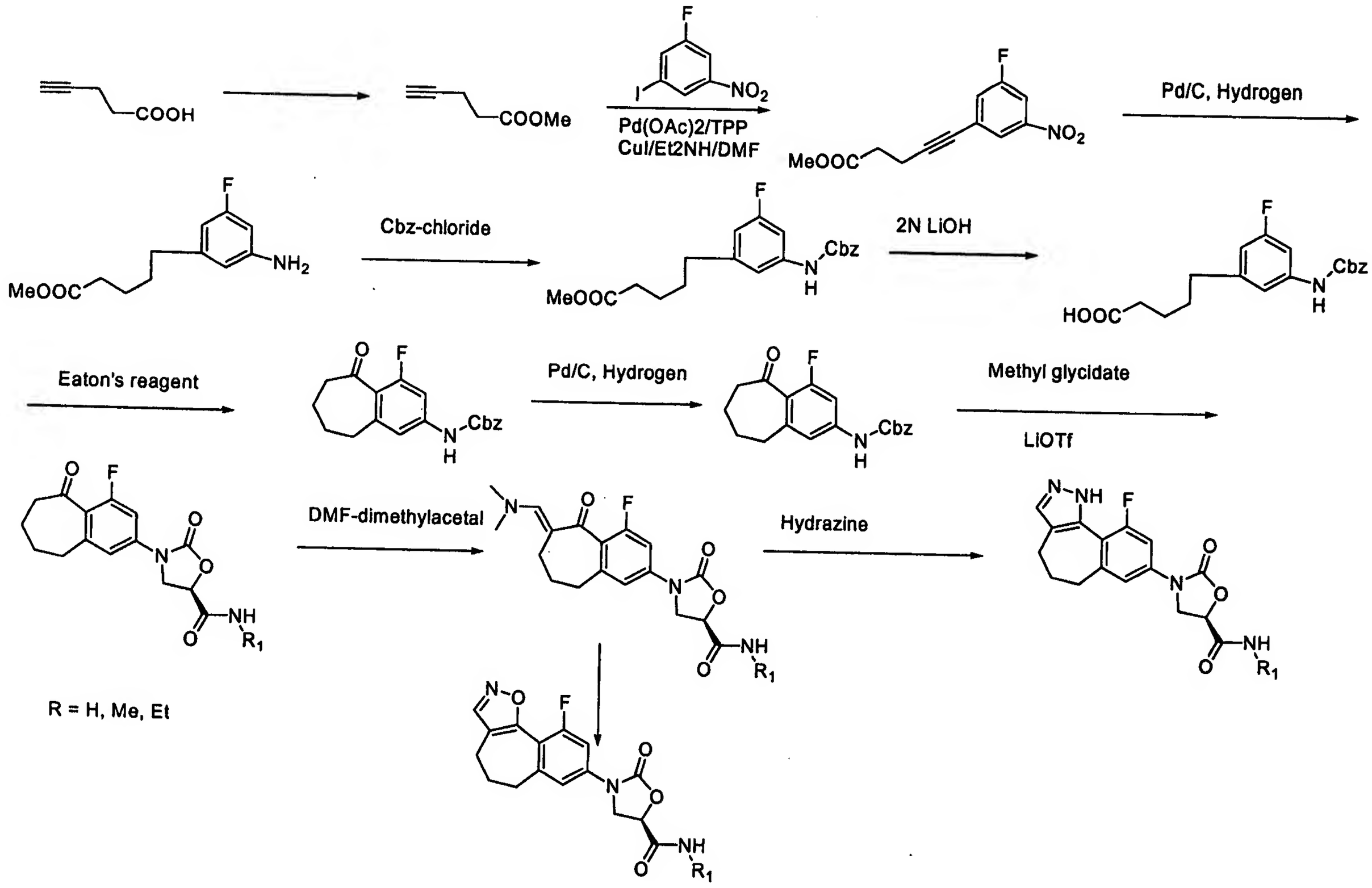

COOH
COOMe
Pd(OAc)2/TPP
CuI/Et2NH/DMF
Pd/C, Hydrogen
Cbz-chloride
2N LiOH
Eaton's reagent
Pd/C, Hydrogen
Methyl glycidate
LiOTf
DMF-dimethylacetal
Hydrazine
R = H, Me, Et

FIGURE XXIII

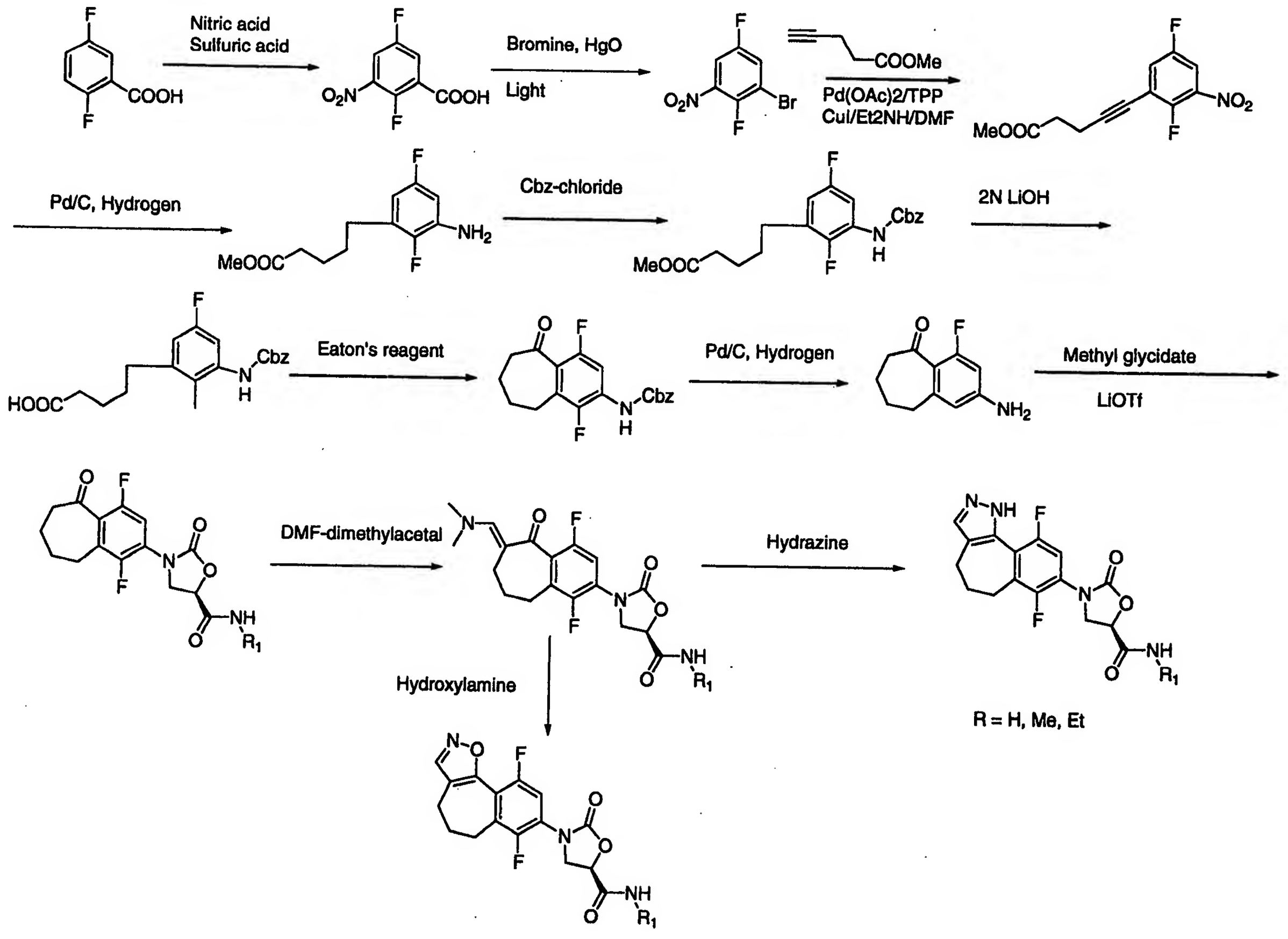


FIGURE XXIV

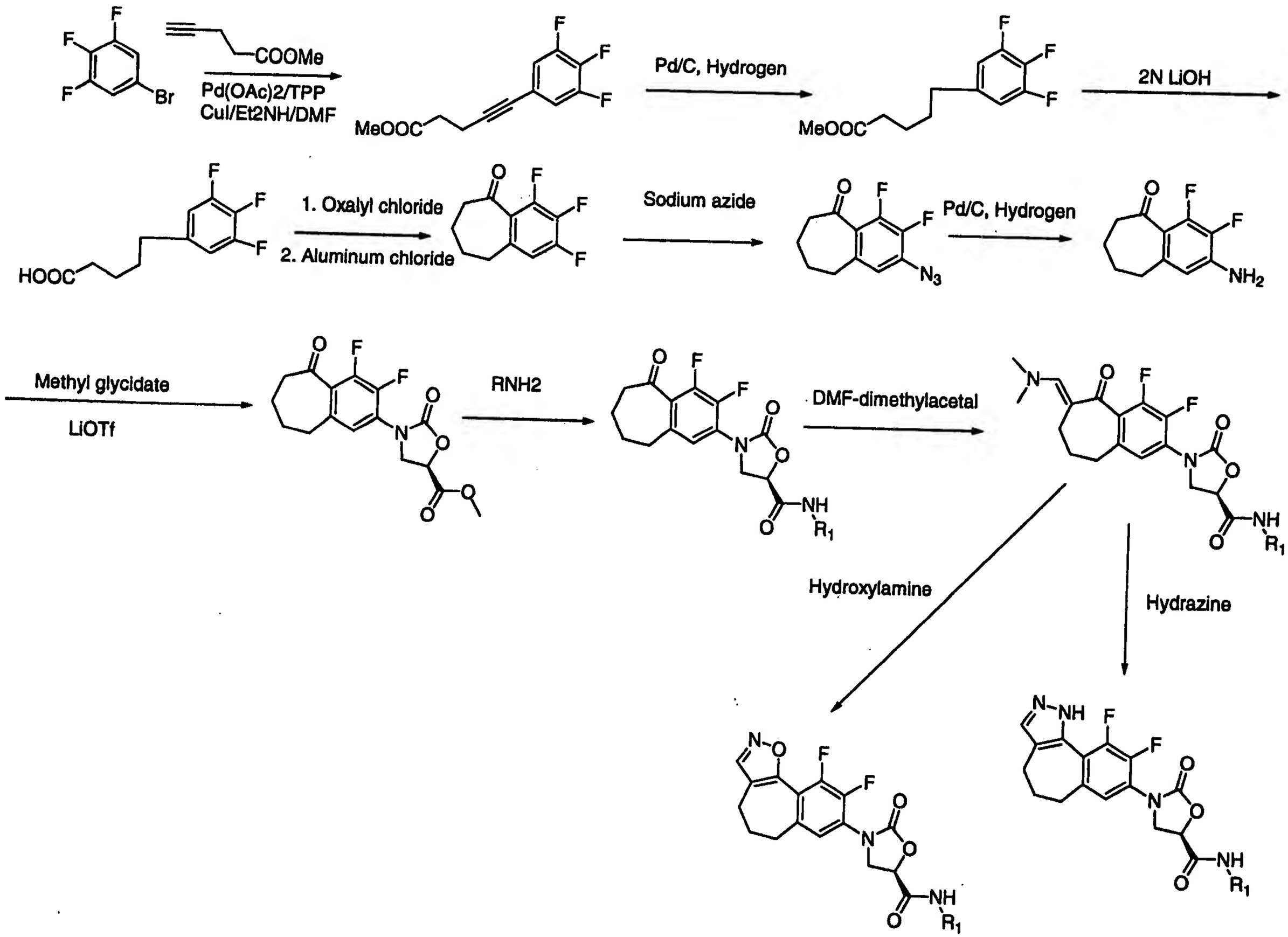

COOMe
Pd(OAc)2/TPP
CuI/Et2NH/DMF
Br
MeOOC
Pd/C, Hydrogen
2N LiOH
HOOC
1. Oxalyl chloride
2. Aluminum chloride
Sodium azide
N3
Pd/C, Hydrogen
NH2
Methyl glycidate
LiOTf
RNH2
DMF-dimethylacetal
NH
R1
Hydroxylamine
Hydrazine
N-O
N-NH

FIGURE XXV

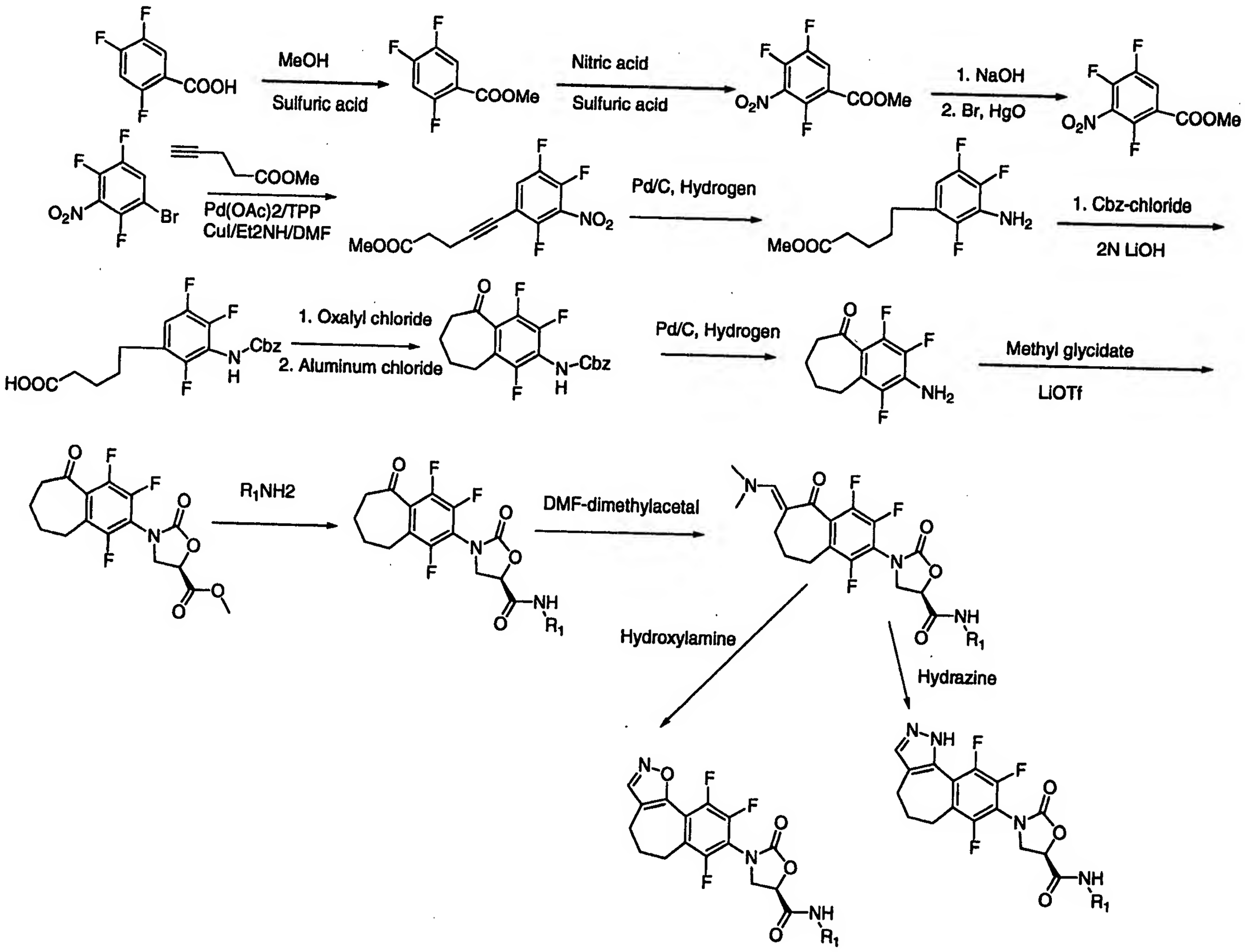

MeOH
Sulfuric acid
Nitric acid
Sulfuric acid
1. NaOH
2. Br, HgO
COOMe
Pd(OAc)2/TPP
CuI/Et2NH/DMF
Pd/C, Hydrogen
1. Cbz-chloride
2N LiOH
1. Oxalyl chloride
2. Aluminum chloride
Pd/C, Hydrogen
Methyl glycidate
LiOTf
R1NH2
DMF-dimethylacetal
Hydroxylamine
Hydrazine

FIGURE XXVI

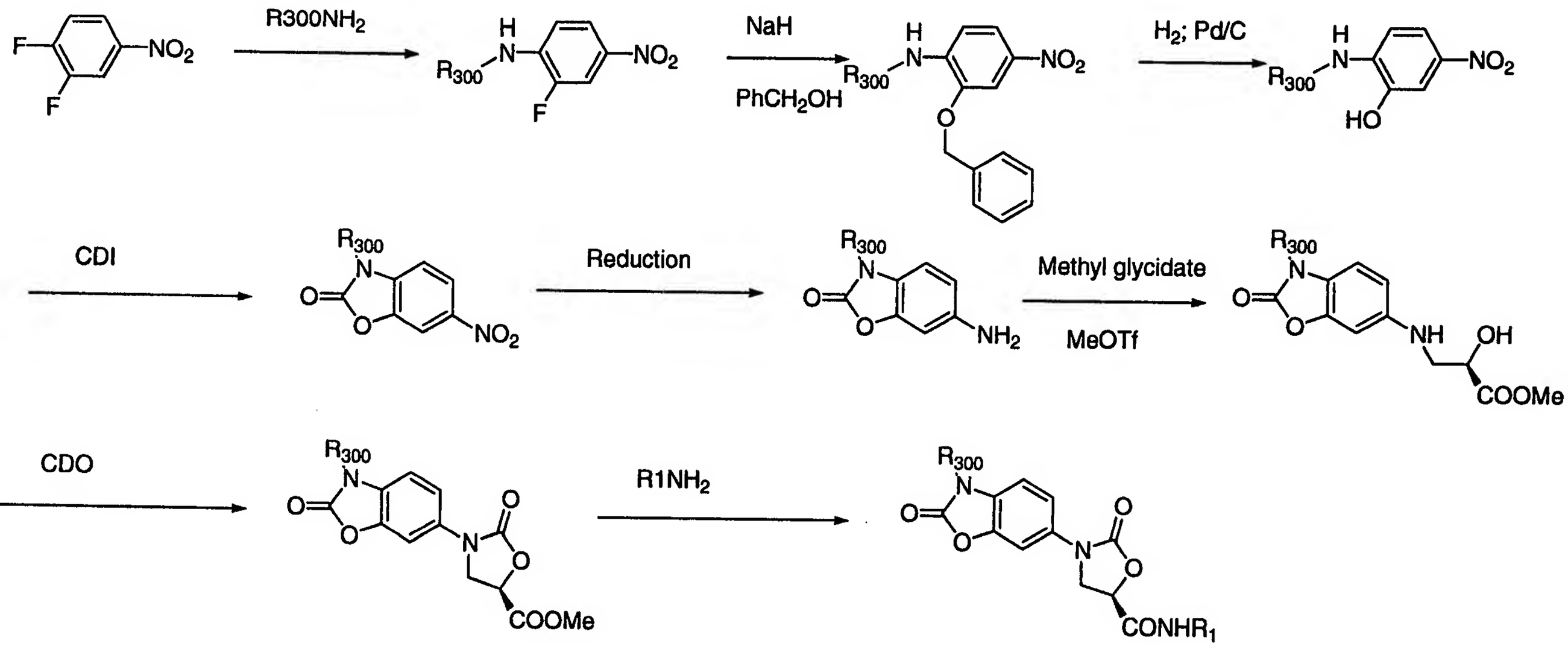

F
NO2
F
R300NH2
H
N
R300
NO2
F
NaH
PhCH2OH
H
N
R300
NO2
O
H2; Pd/C
H
N
R300
NO2
HO
CDI
R300
N
O
O
NO2
Reduction
R300
N
O
O
NH2
Methyl glycidate
MeOTf
R300
N
O
O
NH
OH
COOMe
CDO
R300
N
O
O
O
N
O
COOMe
R1NH2
R300
N
O
O
O
N
O
CONHR1

FIGURE XXVII

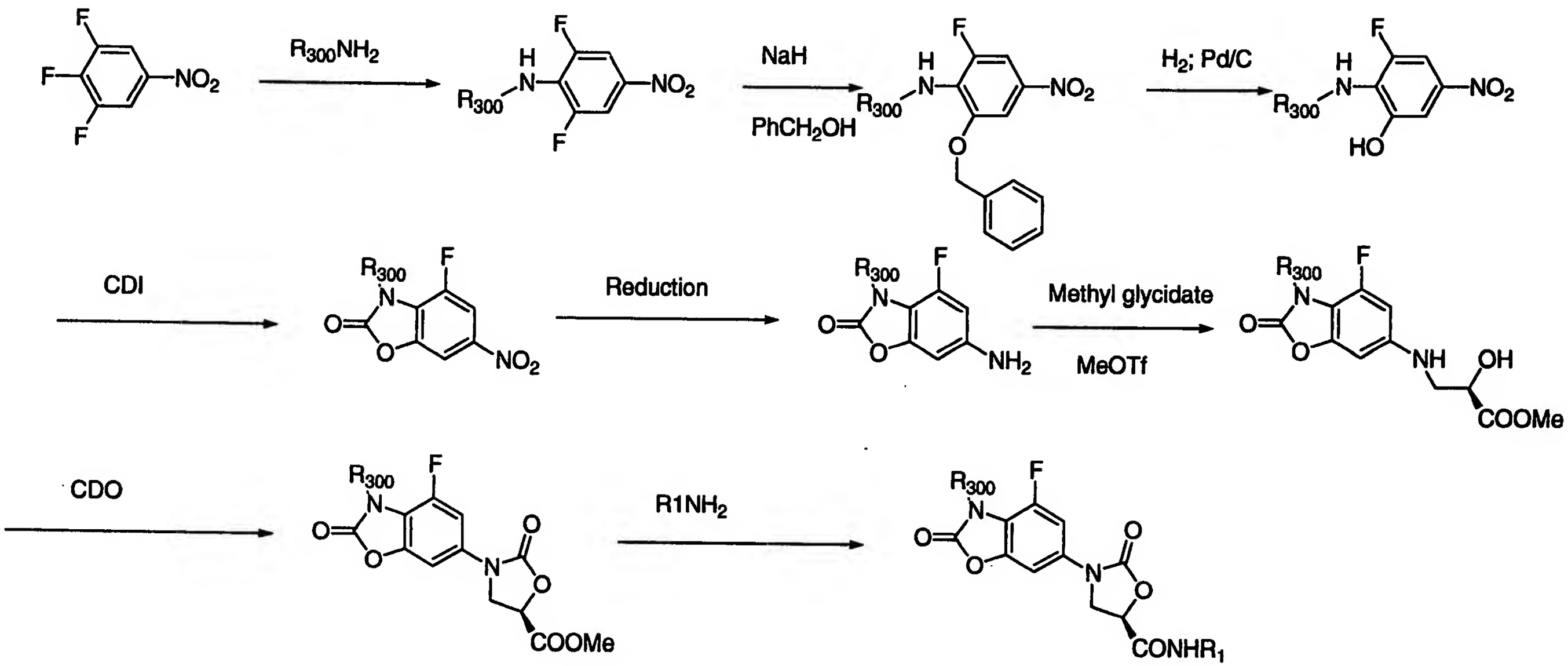


FIGURE XXVIII

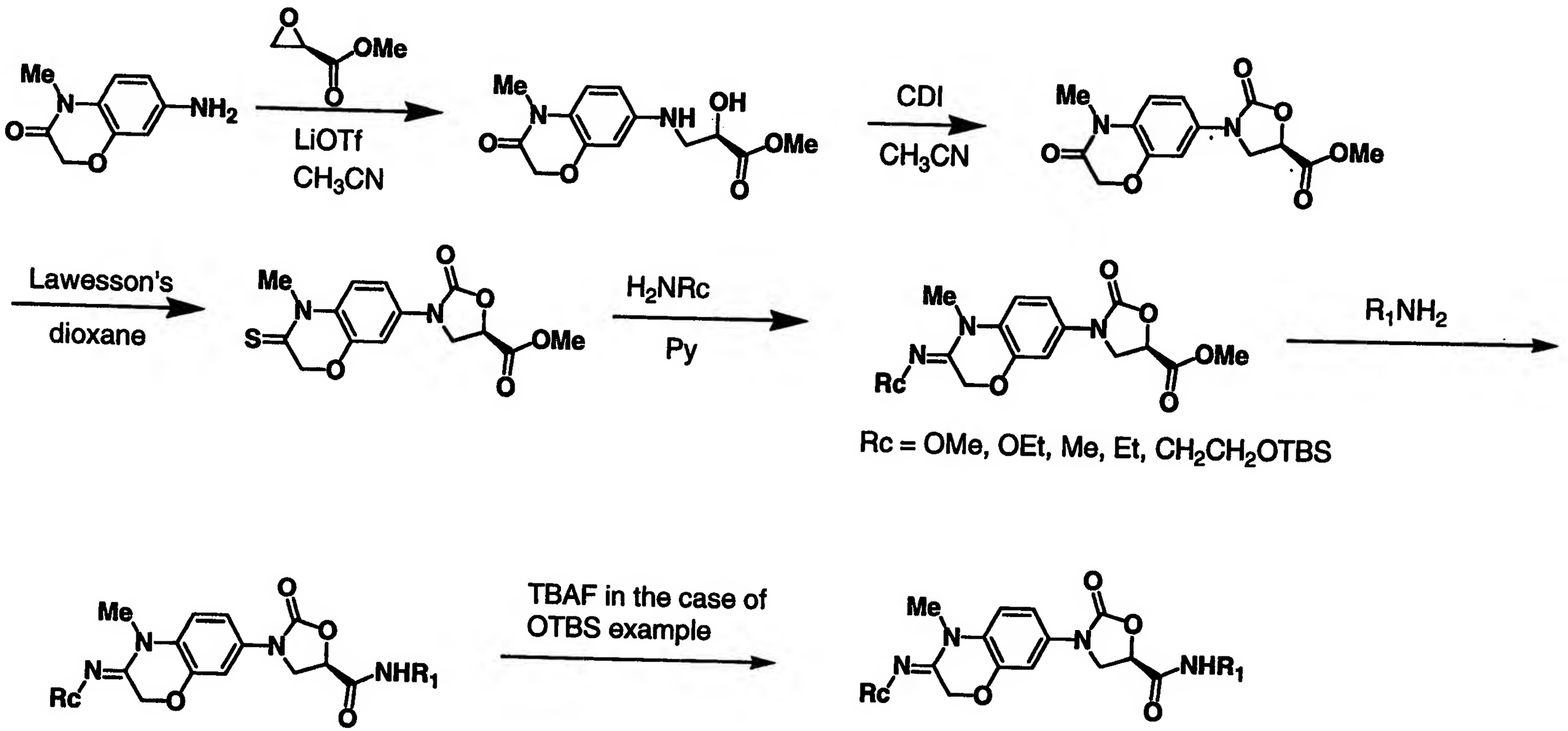
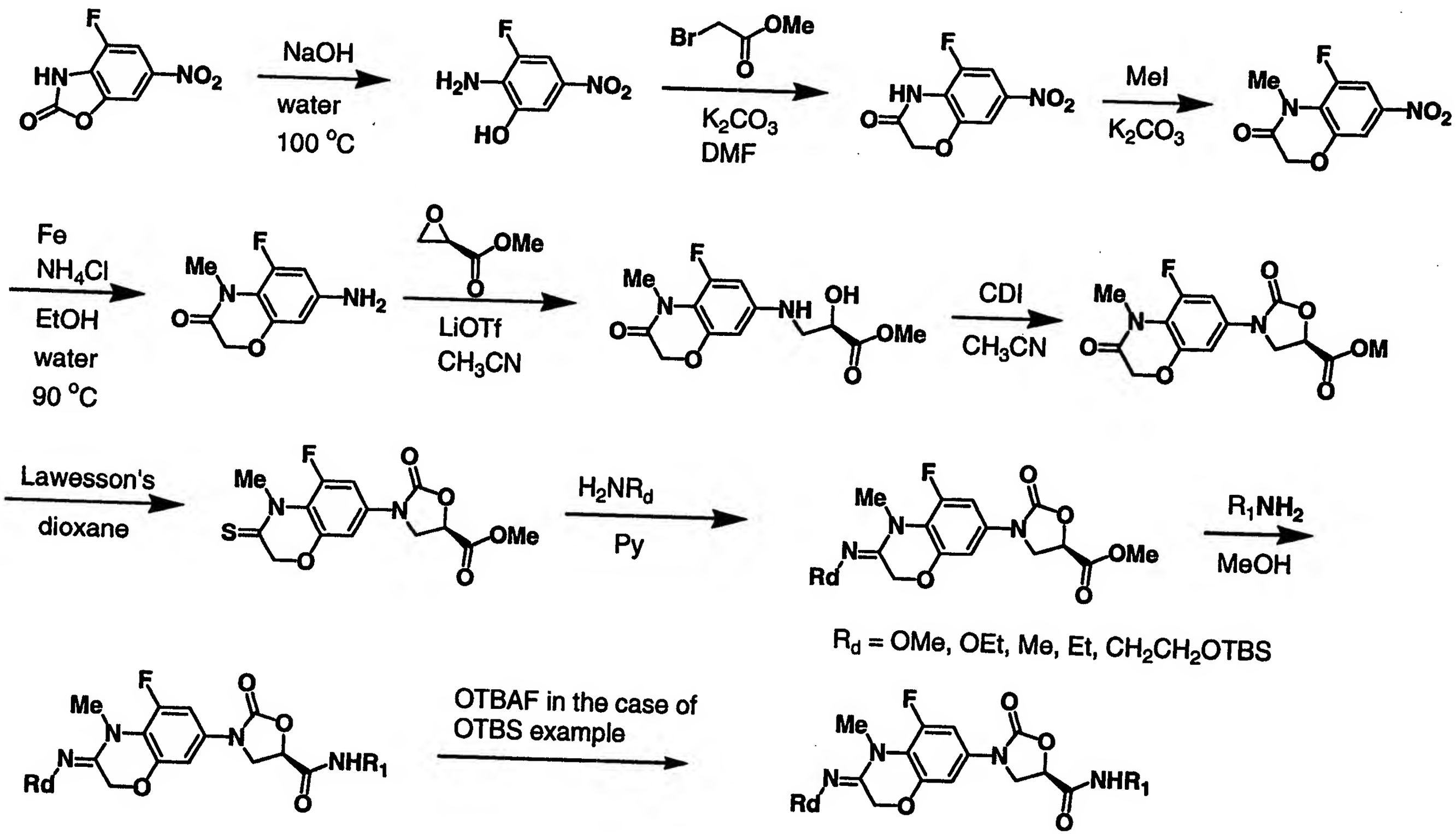


FIGURE XXIX


NaOH
water
100 °C
K2CO3
DMF
MeI
K2CO3
Fe
NH4Cl
EtOH
water
90 °C
LiOTf
CH3CN
CDI
CH3CN
Lawesson's
dioxane
H2NRd
Py
R1NH2
MeOH
Rd = OMe, OEt, Me, Et, CH2CH2OTBS
OTBAF in the case of
OTBS example